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THE DISTINGUISHED SOVIET SCIENTIST, ILYA ILYICH CHERNYAEV

COMMEMORATION OF HIS SIXTIETH BIRTHDAY)

A. V. Babaeva

The largest school in the world of chemists specializing in inorganic complexes was created in Russia by that talented Russian scientist L. A. Chugaev. Chugaev died young but his students continue the work that he started; they have developed, extended and consolidated the chemistry of complex compounds in the service of the socialist Fatherland.

The outstanding student of L. A. Chugaev is academician Ilya Ilyich Chernyaev, who made many discoveries and carried out many investigations in the field of complex compounds of the platinum metals. He is rightly regarded as one of the creators of refining technology in the Soviet precious metals industry and has tirelessly exerted himself together with his students in furthering its interest. With the name of I. I. Chernyaev is associated the creation of a new and advanced method for purification of platinum, its separation in the highest degree of purity, the preparation of pure osmium, a method for extracting platinum metals from poor ores, the development of a series of analytical methods for the very complicated analysis of noble metals, and the solution of many other critical problems of the industry.

It is difficult to overestimate the fruitful activity of I. I. Chernyaev and his school in the field of refining of platinum and its congeners. The USSR leads the world in the extraction and processing of platinum ores, and the technology of refining of precious metals is the pride of our country. The services of I. I. Chernyaev and his school have been recognized by the Government. It must be stated that their achievments were dependent on the previous extensive and penetrating investigations of the chemistry of complex compounds of the precious metals.

Among the many investigations carried out by Ilya Ilyich, special interest attaches to those on compounds of bi- and quadrivalent platinum containing a nitro group, since these investigations led to his discovery in 1926 of the law of the trans-effect.

The trans-effect law represents an important extension of the coordination theory of the structure of complex compounds, based on the systematic development of the ideas of V. V. Markovnikov about the interaction of the component parts of molecules.

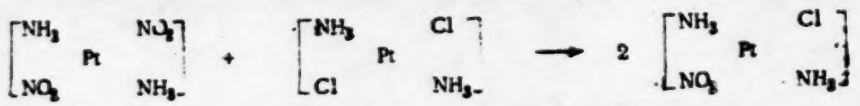
Although paying due respect to the coordination theory, I. I. Chernyaev nevertheless considered that it is too "geometrical" and lacks dynamism. On the basis of this theory, capable as it is of predicting the number of possible geometrical configurations of a molecule, it is impossible to draw any conclusions as to the interaction of the components of the coordination sphere or, in turn, any conclusions about the mode of synthesis of the compounds.

When investigating various platinum compounds containing nitro groups, I. I. Chernyaev observed a substitution reaction at the linkage of the central atom with substituents located in the trans-position to the nitro-groups. As a result of the study of diverse reactions of complex compounds of bivalent platinum, I. I. Chernyaev established that the loosening and strengthening of the bond of a given substituent with the central atom depends on the nature of the group or atom present in the trans-position, acidic groups producing a greater trans-action than neutral molecules. Further work in collaboration with A. D. Gelman widened our knowledge of the phenomenon in that it was observed that such unsaturated molecules as ethylene, propylene, nitric oxide and carbon monoxide are characterized by a marked trans-effect in complex compounds. It was therefore inferred that the trans-effect of substituents increases with increased covalence of the bond.

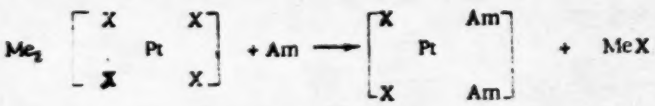
In respect of trans-activity, inner-sphere substituents are arranged in the following approximate order:

$$R_2S > NO_2 > I > Br > Cl > F > OH > RNH_2 > NH_3 > H_2O$$

Examination by I. I. Chernyaev of inner-sphere reactions of such well-investigated complex compounds as compounds of cobalt and chromium showed that the positions of maximum activity are arranged in the inner sphere in accordance with the principle of the trans-effect. I. I. also explained the exchange reaction of nonelectrolytes, discovered by him, on the basis of the trans-effect:

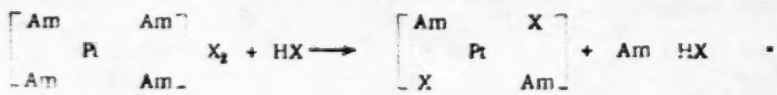


The cis- and trans- forms of platinum compounds can be traced to a single cause on the basis of the trans-effect. Indeed, the formation of cis-diammines from acido complexes by reaction with ammines:



(cis-form)

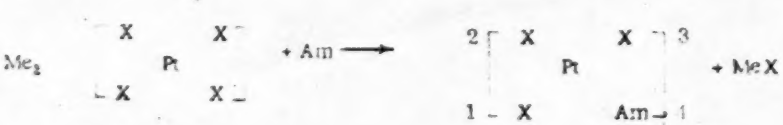
and the formation of trans-diammines from tetrammines by the action of acids:



(trans-form)

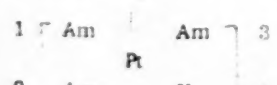
become comprehensible if we take the trans-effect into account.

The formation of a cis-diammine $[(AmX)_2\ Pt]$ naturally proceeds through the formation of the monoammine:



the acid substituents in positions 1 and 3 in this monoammine being mutually labile, whereas the substituent in position 2 is in a more stable form since it is located opposite to a trans influencing ammine group. Due to this, the reaction of further substitution by the ammine must proceed at positions 1 or 3, which are completely equivalent, and must lead to a diammine with trans-configuration.

The very first stage in the action of acids on tetrammines of bivalent platinum is the formation of the triammine (A). In this molecule the most labile



(A)

ammine is the group in position 1 since it is exposed to the trans effect of the acid group, and therefore the further action of acid causes substitution of this very ammine and this leads to formation of a trans-ammine. Thus the trans-effect provided a uniform explanation of the long-known empirical cis- and trans law.

Guided by the discovery of the principle and pursuing the aim of precise determination of the place of reaction of the substituent in the inner sphere of the complex compound, L. L. Chernyaev synthesized triammines with the general formula $[A_1A_2A_3NO_2Pt]X$. He succeeded in obtaining the compound $[Py \cdot NH_3 \cdot NH_2OH \cdot NO_2Pt]X$ in three geometrically isomeric forms.

For the compound $[C_2H_4(NH_2)_2 \cdot NH_3ClBrNO_2Pt]X$ the coordination theory predicts six isomers. The synthesis of these six compounds, if attempted at random, would require an enormous period of time and might not even be successful. L. L. Chernyaev synthesized five out of the six possible geometrical isomers.

L. L. Chernyaev and his pupils carried out a series of investigations of the optical activity of complex compounds of tetravalent platinum arising out of their molecular asymmetry. A series of compounds of these types was resolved into their optical antipodes with the aim of confirming the correctness of the configuration attributed to the tetrammines and triammines of quadrivalent platinum. This was no light task. The actual synthesis of the racemates of these compounds was only possible by utilization of the law of the trans-effect.

Illustrative of the fruitfulness of the application of the trans-effect is the large number of USSR publications on the synthesis of complex compounds of various metals and in particular of complex compounds of metals of the platinum group.

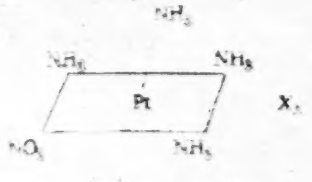
What is the precise physical significance of the phenomenon of the trans-effect? Is it characteristic only of compounds with a coordination structure or has it a more general significance? Is the trans-effect peculiar to compounds in the crystalline state, or is it the consequence of interaction with a solvent, since the trans-effect is almost invariably associated with reactions in solutions and predominantly in water? None of these problems has yet been fully solved.

In the first years following its discovery, the author of the trans-effect explained it on the basis of the Werner hypothesis of "passive resistance" developed in the inner sphere of the complex compound and stabilizing this sphere. According to L. L. Chernyaev, this "passive resistance", possessing not only magnitude, but also direction is concentrated in that part of the sphere where the acid substituent is most firmly bonded to the central atom, so that the "passive resistance" is diminished in the opposite side of the sphere, i.e. in the trans-position to the acid substituent, with consequent loosening of the bond with the central atom.

A. A. Grinberg and B. V. Nekrasov made almost simultaneous attempts at a physical treatment of the trans-effect. They regard the trans-effect as a special case of counterpolarization, associated in the case of differently characterized and differently polarized substituents with anisotropy of the field of the central atom, creating favorable conditions for lability of the substituent located in the trans position to the substituent with the highest polarization. There are a series of objections, however, to this treatment since it makes assumptions that do not always accord with the facts.

At the present time, L. L. Chernyaev regards the trans-effect as an inner sphere catalysis with the electrons playing a directive part. He attributes the trans-effect to all atoms, molecules and electrons without exception. In complex compounds the central atom also possesses a trans-effect. "The universality of the trans-effect" writes Chernyaev – "requires that the central atom should also possess the same catalytic bond as exists between the atoms of the molecules linked to it".

In compound (B) not only does the nitro group render labile the opposite $Pt{-}NH_3$ bond, but the trans-effect of the platinum atom leads to labilization of the $N{-}H$ bond and to equiponderant detachment of a proton from ammonia and transformation of the ammonia into an amino group.



(B)

$$RNH_3 \rightleftarrows RNH_2^- + H^+$$

This phenomenon, observed by Kleve and later by Chugaev in the platinum pentammines, was also observed by Chernyaev in a series of other amino compounds of quadrivalent platinum and in hydroxylamino compounds of bivalent platinum; pupils of L. L. Chernyaev also observed it in acetoxime compounds of bivalent platinum.

The aquo-hydroxo-reactions $RH_2O \longrightarrow ROH^- + H^+$, which are known not only in the case of complex compounds of metals of the platinum group, but also in that of compounds of chromium and cobalt, must in Chernyaev's opinion be explicable also on the bais of the trans-effect of the central atom. Even if the amino reaction and the hydroxo reaction do not always take place in presence of amines and water in the inner sphere of the complex compound, this can be explained not by the absence of the trans-effect of the central atom but possibly by the geometrical arrangement of the components of the molecule which is such as to protect the hydrogen of the water and amines against the trans-effect. Also illustrative of the trans-effect of the central atom, in Chernyaev's opinion, is the behavior of the oxygen in the nitro group of complex compounds, for example, in $[(NH_3)_5NO_2Pt]X$. Being subject to the trans-effect of the platinum, it is more labile than the oxygen in the free NO_3^- ion, and that is why the nitro group in complex compounds is also reduced by hydrogen to the amino group, while heating of complex compounds containing a nitro group with ammonium chloride leads to the reaction of N. N. Zinin:

$$RNO_2 + NH_4Cl \longrightarrow RCl + N_2 + H_2O$$

I. I. Chernyaev regards the trans-effect as a general principle which also accounts for the limited magnitudes of the coordination number and the difference in the behavior of the inner-sphere and outer-sphere groups. Concerning the latter, the author of the trans-effect writes: "since the effect of the central atom is to cause weakening of the existing chemical bonds in the combined molecule, this can make all the more impossible the formation of chains from the molecules linked to the central atom".

All this, however, is a long way from revealing the true nature of such a remarkable phenomenon as the trans-effect. "It is only perfectly clear", writes Chernyaev in one of his papers, "that in the field of the chemistry of complex compounds, the principle of the trans-effect is that expression of a unified law of interaction of the atoms constituting a molecule whose clarification for carbon compounds was the dream of V. V. Markovnikov".

For the discovery, expression and application of the law of the trans-effect, I. I. Chernyaev received the Stalin Prize First Class in 1952.

Headed by Academician I. I. Chernyaev, the N. S. Kurnakov Institue of General and Inorganic Chemistry of the Academy of Sciences of the USSR has carried out investigations over a wide front on important problems of physicochemical analysis, complex compounds and the chemistry of metals and salts.

Under the direct supervision of I. I. Chernyaev, the Platinum Section, apart from chemical investigations of complex compounds, is studying their physicochemical and physical properties: electric, magnetic, spectral, crystal chemical, thermochemical, etc., a knowledge of which is necessary for clarification of the nature of the trans-effect and its quantitative characterization. The application of a dominating idea in these investigations is an advantage to the Soviet school of complex chemistry which is not shared by foreign workers.

Investigators who are working on the above-mentioned problems of complex compounds in the laboratories of the Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR are also solving important practical problems in collaboration with industry.

Twenty years ago, at the session of the Academy of Sciences of the USSR devoted to problems of the Ural-Kuzbas, I. I. Chernyaev said: "We must hope that the fusion of theory and practice in the future will lead us to mastery over materials on a scale undreamed by the greatest enthusiasts".

Ilya Ilyich Chernyaev realized this fusion of theory and practice throughout the whole of his scientific activity and his activity as director of the institute.

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THE THERMOCHEMISTRY OF CUPRAMMONIUM COMPLEXES IN AQUEOUS SOLUTION

K. B. Yatsimirskii and Z. M. Grafova

The cuprammonium complex compounds have been the subject of many investigations. These compounds as we know, find extensive practical application. Many workers have studied the equilibria in aqueous solutions of cuprammonium complexes [1, 2, 3,]. These studies have revealed the composition of cuprammonium complexes, have demonstrated the stepwise character of the complex-formation, and have enabled calculation of the instability constants of a series of ions of the type of $Cu(NH_3)_n^{2+}$ (n = 1, 2, 3, 4, 5).

In respect to their thermochemistry, these complex compounds have clearly not been adequately investigated.

About 50 years ago, Bouzat [4] determined the heats of mixing of aqueous solutions of ammonia and copper sulfate. Experiments were performed at temperatures of 10-13° C; the data obtained relate to a narrow range of ammonia concentrations (0.5 to 1M).

Quite recently, Fyfe [5] determined the heat of mixing of a 1 M solution of amonia with a copper salt solution at temperatures of 14-17° and obtained a value close to that found by Bouzat.

It may be pointed out that Fyfe erroneously regards this value as the heat of formation of $Cu(NH_3)_4^{2+}$ from the copper ion and aqueous ammonia. Actually a 1 M solution of ammonia only contains 77% of the copper in the form of $Cu(NH_3)_4^{2+}$ [6], the remaining 23% being in the form of $Cu(NH_3)_3^{2+}$.

Data for more concentrated solutions of ammonia are lacking in the literature. There are no data that permit evaluation of the possibility of formation of mixed complexes of the type of $[Cu(NH_3)_n(OH)_m]^{2-m}$. However, the probability of formation of such complexes is extremely high, since complex ions of the type of $Cu(NH_3)_4^{2+}$ and $Cu(OH)_4^{2-}$ are distinguished by great stability [7].

EXPERIMENTAL

The previously described apparatus and procedure [8] were used for determination of the heat of mixing of a solution of copper sulfate with solutions of ammonia, and also of solutions of cuprammonium complexes with solutions of caustic alkali.

In the first series of experiments the calorimeter was filled with solutions of ammonia of various concentrations (from 0.5 to 6.9 M). One and the same volume of ammonia solution (500 ± 1 ml) was used in all the experiments. The weight of the test solutions was determined on a technical balance.

A 0.304 M copper sulfate solution (the copper content of the solution was determined by the electrogravimetric method) was poured into glass ampoules with a small glass side bulb (the weight of copper sulfate was determined on an analytical balance). The ammonia was then introduced into the calorimetric liquid and crushed against the side wall of the Dewar vessel after establishment of a uniform temperature gradient. In view of the fact that the duration of the main action did not exceed 3-4 minutes, the radiation correction was found by a graphical method. The water number of the calorimeter was found from the heat of solution of a definite weight of chemically pure potassium chloride and was 66 ± 0.5 cal/g.

The heat capacity of aqueous solutions of ammonia has been determined by Vlevsky and Kalgorodov [9] who found that over the whole range of concentrations the heat capacity is equal to unity with insignificant variations in the third decimal place. The values of Vlevsky and Kalgorodov were subsequently confirmed [10].

Introduction into the solution of minute amounts of a copper salt (the concentrations of $Cu(NH_3)_n^{2+}$ did not exceed 0.004 M) could not appreciably change the heat capacity of the solution, and therefore we assumed in all cases that the heat capacity of the prepared solutions was unity. The deviation between parallel exper-

iments did not exceed ± 3%. A summary of the results obtained is given in Table 1.

TABLE 1

Heat of mixing of solutions of copper sulfate with solutions of ammonia

Prep. No	Ammonia conc (moles/l.)	Amt. of copper (g)	Temp. change with radiation correction	Radiation correction	Heat capacity of calorimeter (in kcal)	Heat of mixing (in kcal per mole Cu)	Mean value of Δ H (in kcal)
1	0.5	0.1342	0.0676	0.0016	565.9	18.5	−18.5
2	1.0	0.1149	0.0662	0.0009	561.4	21.0	−20.7
		0.1328	0.0732	0.0028	562.7	20.4	
3	2.0	0.1290	0.0826	0.0005	560.9	23.4	−23.3
		0.1146	0.0736	0.0010	557.2	23.2	
4	3.8	0.1216	0.0894	0.0005	552.5	26.5	−26.8
		0.1294	0.0992	0.0014	552.7	27.1	
5	4.9	0.1075	0.0846	0.0015	550.6	28.0	−28.0
6	6.9	0.1442	0.1232	0.0048	542.2	30.1	−30.2
		0.1342	0.1174	0.0057	540.8	30.6	
		0.1051	0.0908	0.0030	539.3	30.1	

In a second series of experiments the calorimetric liquid was a solution of a cuprammonium complex in ammonia. The initial concentration of ammonia in all cases was 0.68 M, but the concentration of the cuprammonium complex was varied from 0.00160 to 0.00573 M. A 4 N solution of NaOH was poured into ampoules.

The weight of the NaOH solution was determined on an analytical balance. After a uniform temperature gradient had been established the ampoule was crushed. All measurements and calculations were performed as in the first series of experiments.

In preliminary experiments it was established that on crushing an ampoule containing alkali solution in 0.68 M ammonia no temperature change was observed, and therefore the absorption of heat is bound up with reaction between the cuprammonium complex and the alkali. Experimental results are set out in Table 2.

EVALUATION OF RESULTS

The heats of mixing of solutions of copper salts and ammonia at relatively low concentration of ammonia (0.5–1.2 M) were determined by Bouzat [4] and us. The values that we obtained, notwithstanding the different experimental temperature substantially agreed with those of Bouzat. With increasing ammonia concentration the heats of mixing rise very considerably.

On comparing the results with our data for nickel salts we see that at low ammonia concentrations the heats of formation of cuprammonium complexes in aqueous solution only slightly exceed in absolute value the heats of formation of nickel ammonium complexes [8].

Sharp differences in heats of mixing are observed at high ammonia concentrations (see diagram). In the case of formation of cuprammonium complexes the value of the heat of mixing does not tend to approach any definite value, but continuously rises. This course of the curve may be explained by the fact that side by side with the $Cu(NH_3)_4^{2+}$ complex there is formed in solution the complex ion of $Cu(NH_3)_5^{2+}$, which is not characterized by special stability.

TABLE 2

Heats of Mixing of Solutions of Cuprammonium Complex with Alkali Solution

No. of expt.	Wt. of solution (g)	Concentration of cuprammonium complex in solution (moles/liter)	Temp. change with correction for radiation	Correction for radiation	Heat capacity of calorimeter (cal)	Heat of mixing (kcal/mole)	Mean value of ΔH
1	5.7816	0.00160	−0.0070	0.0009	558.3	−3.08	
2	5.7934	0.00305	−0.0122	0.0002	558.3	−2.93	+3.03
3	5.7952	0.00573	−0.0121	0.0009	559.3	−3.00	

According to Bjerrum the equilibrium constant of the reaction $Cu(NH_3)_5^{2+} \rightleftharpoons Cu(NH_3)_4^{2+} + NH_3$ is 0.3. Consequently even in 7 M ammonia solution there is present ..., 32% $Cu(NH_3)_4^{2+}$ and 68% $Cu(NH_3)_5^{2+}$.

Another conspicuous feature is the marked difference between the heats of formation (from the copper ion and ammonia in aqueous solution) of the complex ions of $Cu(NH_3)_4^{2+}$ and $Cu(NH_3)_5^{2+}$. Whereas for the former ion $\Delta H > -19$ kcal, for the second it is < -30 kcal. Addition of the fifth molecule of ammonia to the tetrammine complex is accompanied by an extremely large thermal effect ($\Delta H < 11$ kcal). There is no parallelism between the successive heats of addition of molecules of ammonia and the change of standard thermodynamic potential. Furthermore, an inverse dependence is observed in the formation of ammoniacal complexes of copper and nickel: the relative stability of the successively formed complexes diminishes, but the successive heats of addition of ammonia molecules rise in absolute value.

Consequently, the change of entropy with successive addition of ammonia molecules does not remain constant but continuously diminishes.

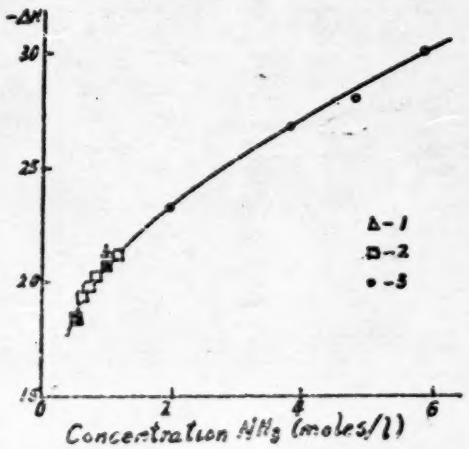

Diagram. Heats of mixing of solutions of copper salts and ammonia. 1. Fyfe's data; 2. Bonzat's data; 3. our data.

The occurrence of a considerable thermal effect during mixing of solutions of caustic alkali with solutions of a cuprammonium complex is evidence, in our opinion, of a reaction in the system which leads to formation of a mixed hydroxo-ammono- complex. The value of the heat of mixing remains constant with changing concentration of cuprammonium complex. Formation of the mixed hydroxo-ammono- complex is accompanied by absorption of heat and, consequently, by an increase of entropy.

SUMMARY

1. The heats of mixing of solutions of $CuSO_4$ with ammonia solutions were determined over a wide range of concentrations (from 0.5 to 6.9 M).

2. The heat of mixing of solutions of NaOH with solutions of cuprammonium complex (0.0016 to 0.0057 M) were determined.

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*See Consultants Bureau English Translation, p. 1765.

PHYSICOCHEMICAL ANALYSIS OF THE BINARY SYSTEMS OF UREA AND ALIPHATIC ACIDS

N. Z. Rudenko and D. E. Dionisyev

The aim of the present investigation was the clarification of the nature of the reaction between urea and acetic, butyric and chloracetic acids in the liquid phase. The choice of components was dictated by the desire to determine the effect of chain lengh and of introduction of electronegative substituents on the character of the reaction with urea. Moreover, a study of systems of urea with aliphatic acids is interesting in that urea is one of the most important products of nitrogen metabolism in the animal organism, and in that during digestion the fats are broken down into their components, the fatty acids undergoing further breakdown with formation of lower acids.

We studied the density, viscosity and electric conductivity at three temperatures. The procedure was as previously described [1].

The viscosity was expressed in centipoises, the concentration in mole-%.

The system urea-acetic acid has been often investigated by the fusibility method [2-6]. All the investigators quite definitely established the presence in the system of the compound $CO(NH_2)_2 \cdot 2CH_3COOH$, which dissociates considerably even at the melting point.

The acetic acid used in this work had m.p. 16.6° after purification by freezing; the urea had m.p. 132.7° after repeated crystallization from water.

Viscosity, density and electric conductivity were studied at 80, 90, and 100°. In the system containing more than 70 mole-% urea, appreciable decomposition with loss of carbon dioxide occurred even at 100°.

In Fig. 1 is plotted the dependence of viscosity on concentration. The viscosity isotherms of the system are curves slightly convex to the axis of concentration. The dependence of viscosity on temperature decreases with increasing concentration of acetic acid.

The curves of density versus concentration (Figure 2) are slightly convex to the axis of composition.

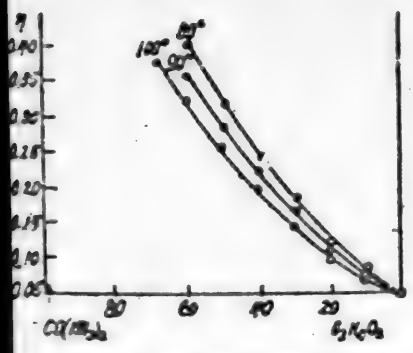

Fig. 1. Viscosity of the system urea-acetic acid.

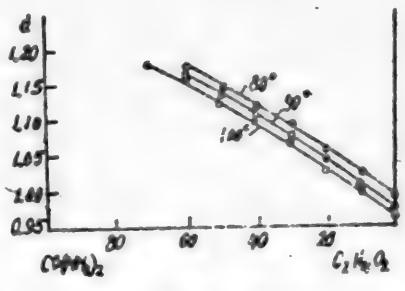

Fig. 2. Specific gravity of the system urea-acetic acid.

Fig. 3 contains plots of electric conductivity (corrected for density) versus composition. These curves are similar to those of the specific electric conductivity, except that they are more convex to the axis of concentration.

We only give the isotherms of electroconductivity corrected for viscosity ($\eta\kappa$) on the assumption that, with all their defects such isotherms are more reliable criteria of the processes taking place in the system than specific electric conductivity curves.

System urea-butyric acid has been studied by the fusion method by A. G. Bergman and M. N. Kuznetsova [5]. They established the absence of chemical reaction.

Chemically pure butyric acid was used. It was dried for a long period over anhydrous copper sulfate and then distilled three times with a dephlegmator. B. p. 197.6° at 764 mm.

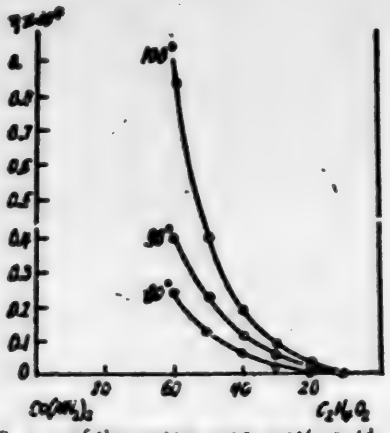

Fig. 3. η_K of the system urea-acetic acid.

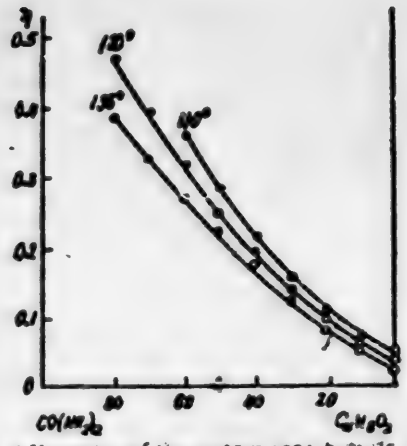

Fig. 4. Viscosity of the system urea-butyric acid.

The viscosity, density and electric conductivity were measured at temperatures of 110, 120, and 135°. Mixtures containing more than 80 mole-% urea decomposed even at 120° with evolution of carbon dioxide.

In Figure 4 is plotted the dependence of viscosity on concentration of components. The viscosity isotherms are slightly convex to the axis of composition.

The density isotherms are almost rectilinear. Rising temperature very slightly reduces the density of the system, and the numerical values for 110, 120 and 135° are very close. For this reason only the 135° isotherm is plotted in Figure 5.

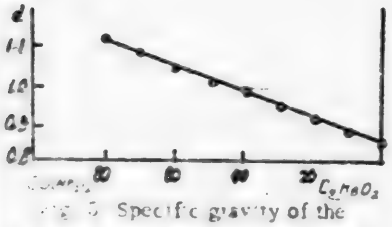

Fig. 5. Specific gravity of the system urea-butyric acid at 135°.

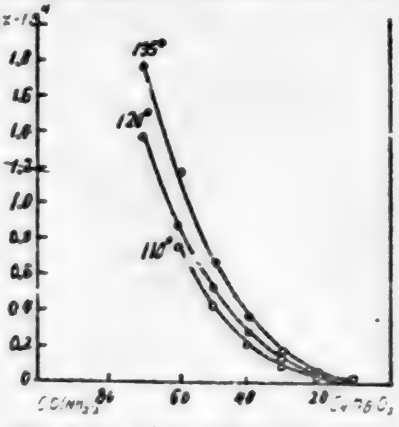

Fig. 6. η_K of the system urea-butyric acid.

The isotherms of electric conductivity corrected for viscosity are curves convex to the axis of composition. The electric conductivity at first rises slowly to 40 mole-% urea and then rapidly with increasing concentration of the latter. The dependence of η_K on composition is plotted in Figure 6.

The system [illegible] acid has been studied by the method by [illegible] who established the formation of a considerable amount of [illegible] ated compound $C_4H_8O_3$, [illegible]

Twice-distilled, chemically pure chloroacetic acid was used. Fractions with b. p. 187° at 720 mm. were sealed in ampoules.

Viscosity, density and electric conductivity were measured at temperatures of 80, 90, and 100°. Mixtures containing more than 80 mole% urea decomposed when heated at above 100°.

The viscosity isotherms shown in Figure 7 are curves convex to the axis of composition. The deviation from additivity is greatest for the 90° isotherm. With rising urea concentration, the temperature coefficient of viscosity increases.

The density/concentration curves are extremely convex to the axis of composition (Fig. 8).

In Figure 9 is plotted the dependence of the electric conductivity, corrected for viscosity, on the composition. In view of the very close numerical values for temperatures of 80, 90, and 100°, the diagram only gives the 100° isotherm; this is a steadily descending curve with convexity to the axis of composition.

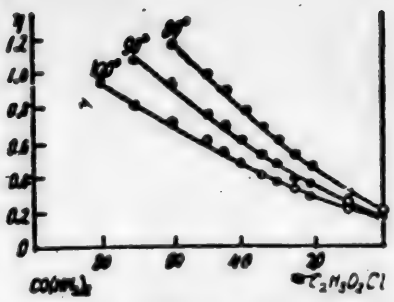

Fig. 7. Viscosity of the system urea-chloroacetic acid.

Fig. 8 Specific gravity of the system urea-chloroacetic acid.

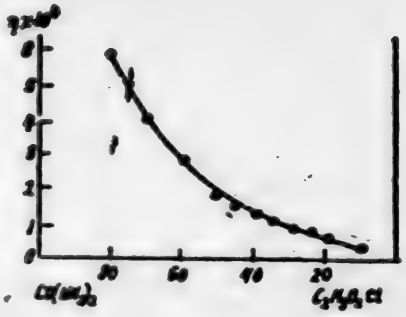

Fig. 9. n_D of the system urea-chloroacetic acid, at 100°.

In this system the electric conductivity changed considerably in the course of time while the viscosity and density of the mixtures remained constant. It is characteristic that the electric conductivity changed in the upward direction only in the fused state. We kept mixtures at room temperature in hermetically sealed vessels for over a month and the electric conductivity remained constant. But when the mixtures were fused, the electric conductivity increased at the mean rate of 2% in 15 minutes. The above values of electric conductivity were determined on freshly prepared mixtures after keeping for 15 minutes in a thermostat.

EVALUATION OF RESULTS

In the system urea-acetic acid the viscosity isotherms are curves which are convex to the composition axis and thus indicate dissociation of an associated component. The electrical conductivity curves likewise do not indicate chemical interaction in the system. The density isotherms (curves convex to the composition axis) point to a slight contraction in the system. Dolezalek [6] is of the opinion that such curves indicate chemical reaction. E. B. Viron [7], however, has established that contraction in a system need not be associated with chemical reaction; he showed that isotherms convex to the composition axis may also occur in the absence of chemical reaction. Hence it follows that the density isotherms must be regarded only against the background of other, more significant, properties.

It may be thought that the compound $CO(NH_2)_2 \cdot 2CH_2ClCOOH$, already strongly dissociated at the melting point, would be wholly dissociated in the liquid phase (at 80, 90, and 100°).

Lengthening of the chain in the acid ought not to increase the tendency toward chemical reaction, as was confirmed for the system urea-butyric acid when this was studied in the liquid phase. The isotherms of viscosity and "converted" electric conductivity, convex to the composition axis, do not point to chemical reaction in the system.

We know that the introduction of chlorine into acetic acid increases its acidity, and this ought to promote its reaction with urea.

However, examination of the isotherms of the properties studied in the liquid phase do not give a direct indication of chemical interaction in the system. It may be thought that the compound $CO(NH_2)_2 \cdot 2CH_2ClCOOH$, also strongly dissociated at the melting point, would be fully dissociated in the liquid phase (at the experimental temperatures of 80, 90, and 100°).

According to the generally accepted interpretation, the viscosity isotherms (convex to the composition axis) reflect dissociation of an associated component in the system. With rising temperature such curves are diminished in convexity and tend to become straight lines. In the system in question the 80° isotherm exhibits the greatest deviation from additivity. It is possible that this abnormality may be provoked by the complexity of the processes taking place in the system and that it is bound up with dissociation of an associated component and the formation of a compound. In that event, with rising temperature there should be found on the viscosity

isotherms an indication of chemical reaction on condition that the fall in viscosity of the mixture caused by dissociation of an associated component with rising temperature is not offset by its increase due to reaction. Unfortunately, it is impossible to check this hypothesis due to intensified decomposition in the system with further rise of temperature.

A too large positive deviation of the density isotherms is, in a way, evidence of chemical interaction in the system.

It is interesting to note that urea with strong inorganic acids gives compounds of the 1:1 type, with bivalent acids compounds of the 1:2 type (2 molecules of urea), and in both cases the urea functions as donor of an electron pair. With weak organic monobasic acids, such as acetic and chloroacetic acids (as well as with phenol), urea gives compounds of the 2:1 type (2 molecules of acid), and should thus function as a donor of two pairs of electrons, but this is very improbable because with inorganic acids urea functions as a monoamine. It is noteworthy that urea gives compounds of the latter type with strongly associated components. It is more probable that also in these compounds the urea functions as a donor of only one electron pair but the pair is accepted by a dimer of the second component. Such a compound will, of course, not be distinguished by great stability, and will decompose with rising temperature. It is conceivable that for this very reason compounds of the 2:1 type are not reflected on the isotherms of properties in the liquid phase of both systems with fatty acids and systems with phenol [1].

SUMMARY

1. Determinations were made of the viscosity, density and electric conductivity of the systems urea-acetic acid, urea-chloroacetic acid at temperatures of 80, 90, and 100°, and urea-butyric acid at 110, 120, and 135°.

2. In all three systems no chemical reaction was detected in the liquid phase.

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*See Consultants Bureau Translation, pages 59 ff.

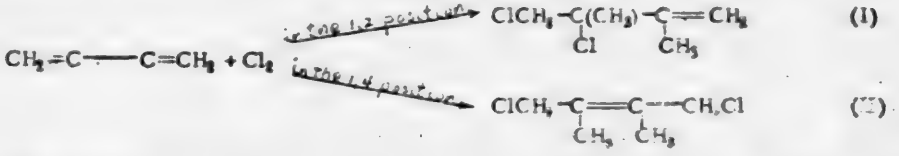
SYNTHESIS OF HYDROCARBONS

XXXIX. 2,3-DIMETHYL-1,3-BUTADIENE DICHLORIDE IN THE SYNTHESIS OF ISOALKENES WITH A CENTRAL DOUBLE BOND

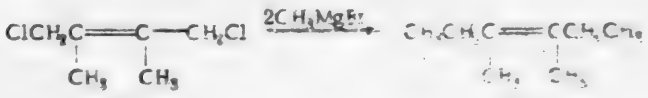
R. Ya. Levina, V. R. Skvarchenko, A. S. Okunevich and E. G. Treshchova

In continuation of our study of the synthesis of olefinic hydrocarbons containing a central double bond by the reaction of dichlorides of conjugated dienes with organomagnesium compounds [1, 2, 3], we have studied in the present paper the reaction between the dichloride of 2,3-dimethyl-1,3-butadiene (diisopropenyl) and organomagnesium compounds (methyl and propyl magnesium bromides).

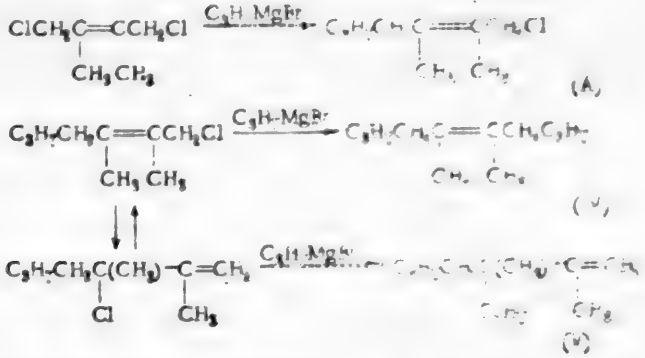
The chlorination of 2,3-dimethyl-1,3-butadiene (here studied for the first time), led to formation of a crystalline dichloride (m.p. 35°), apparently the 1,4-dichloride (I), judging by the analogy with the crystalline 1,4-dibromide of butadiene (bromination of butadiene is known to yield a crystalline 1,4-dibromide and a liquid 1,2-dibromide). The crystalline dichloride could, however, be contaminated with the 1,2-dichloride (I') of 2,3-dimethyl-1,3-butadiene:



Reaction of crystalline diisopropenyl dichloride with methyl magnesium bromide led to formation of 3,4-dimethylhexene-3 (III) (yield 23% of the theoretical) whose structure was confirmed by analysis, by the constants, and by the Raman spectra:

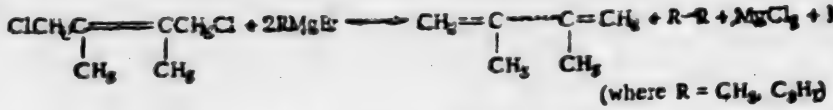


Reaction of the crystalline diisopropenyl dichloride with propyl magnesium bromide gave a mixture of two hydrocarbons (yield 11% of the theoretical): 5,6-dimethyldecene-5 (IV) (90% of the total) and the isomeric α-olefinic hydrocarbon (V) (10%), the latter being due to allylic rearrangement of an unsaturated monochloride—the intermediate product (A).



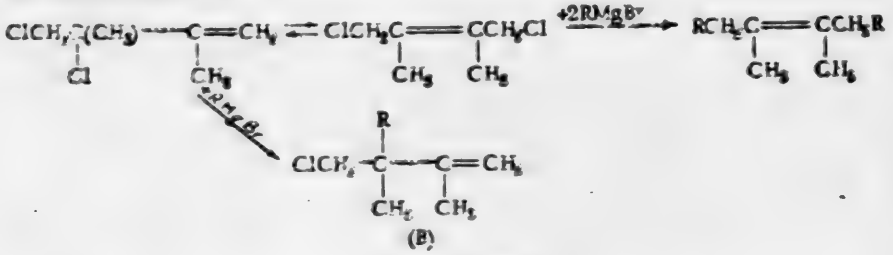
The action of the organomagnesium compound on the unsaturated crystalline diisopropenyl dichloride was also accompanied by a side reaction (which we described in previous communications [1, 2, 3]), leading to recovery

of the original 2,3-dimethyl-1,3-butadiene, while in the case of propyl magnesium bromide, n-hexane was also obtained:



(where R = CH_3, C_3H_7)

Possible contamination of the prepared crystalline 2,3-dimethyl-1,3-butadiene dichloride with 1,2-dichloride need not interfere in the reaction with organomagnesium compounds since during the reaction the 1,2-dichlorides either undergo allylic rearrangement to 1,4-dichlorides [1] (which react further with the organomagnesium compound) or exchange only one atom of chlorine per radical and form the monochloride (B) which does not enter into further reaction:



(B)

EXPERIMENTAL

1. Chlorination of 2,3-Dimethyl-1,3-butadiene (Diisopropenyl)

Chlorination of diisopropenyl was performed at various temperatures (between −15 and −75°). The fall in temperature during cooling is found not to affect the yield of crystalline diisopropenyl dichloride.

Chlorine was introduced into a solution of diisopropenyl (20 g) in absolute ether (25 ml) while cooling the reaction vessel with a mixture of snow and salt. To enable observation of the increase in weight and to determine the completion of the reaction, the reaction vessel was counterbalanced on a balance. The reaction was judged complete when the weight of reaction mixture had increased by the theoretical amount, on the basis of the addition of two atoms of chlorine to the diisopropenyl molecule. The required weight increase of 17 g (for 20 g diisopropenyl) was reached after 30-40 minutes.

After distillation of the ether and fractional distillation of the residue in vacuum (from a flask with a tall deplegmator), the dichloride of diisopropenyl was isolated with b.p. 80-84° (at 18 mm). Almost the whole of the dichloride crystallized when cooled. After pressing and drying on a porous plate, the crystals had m.p. 35°. Yield of crystalline dichloride 62% of the theoretical (300 g diisopropenyl gave 173 g dichloride).

2. Reaction of Crystalline Diisopropenyl Dichloride with Methyl Magnesium Bromide

To methyl magnesium bromide (120 g methyl bromide, 24 g magnesium and 500 ml absolute ether) was gradually added, with water cooling and continuous stirring, a solution of the crystalline diisopropenyl dichloride with m.p. 35° (39 g) in absolute ether at such a speed that the ether only boiled gently. After the whole of the dichloride had been added, the reaction mixture was left overnight. On the next day the stirring was continued for 6 hours at room temperature and for 2 hours on the water bath. Decomposition was effected with dilute acetic acid (10%). After two experiments had been completed, the ether extracts were combined, washed until neutral, and dried with calcium chloride, the ether was distilled off and the residue distilled in a column of 50 theoretical plates. Two fractions were obtained.

The first fraction (product of cleavage of chlorine atoms from the dichloride) was diisopropenyl with b.p. 68.5-69.5° (753 mm); n_D^{18} 1.4380; d_4^{18} 0.7260.

Literature data [4]: b.p. 68.6° (762 mm); n_D^{18} 1.4390; d_4^{18} 0.7262.

The crystalline product of addition of the diene to maleic anhydride had m.p. 79° (from ligroine), in agreement with the literature [5]. A mixed melting test of this adduct with that obtained from the original diisopropenyl did not give a depression.

The yield of diisopropenyl was 15 g or 40% of the theoretical calculated on the initial dichloride.

The second fraction (product of substitution of two atoms of chlorine in the dichloride by methyl groups) had b.p. 119-119.5° (765 mm); yield 13.5 g or 23% of the theoretical (calculated on the initial dichloride).

The second fraction was heated with maleic anhydride in order to eliminate any diisopropenyl and then distilled over sodium in the same column, giving 3,4-dimethylhexene-3 (III), not previously described in the literature. Its constants were:

B.p. 119.2-119.4° (770 mm); n_D^{20} 1.4275; d_4^{20} 0.7415, MR_D 38.89. C_8H_{16}. Calculated: MR_D 38.67.

5.660 mg substance: 17.813 mg CO_2, 7.129 mg H_2O. Found %: C 85.88; H 14.09. C_8H_{16}. Calculated %: C 85.72; H 14.28.

The Raman spectrum of 3,4-dimethylhexene-3 contained the following frequencies (the intensity of the lines was evaluated visually)*:

245 (1; w); 313 (0); 409 (3; w); 421 (0.5); 455 (0.8); 480 (2); 519 (1); 555 (0.5); 585 (2); 600 (1.5); 679 (10); 746 (0); 790 (0.5; w); 846 (1.5); 907 (0); 917 (0); 938 (3.5); 970 (1); 998 (4.5); 1018 (1); 1056 (2.5); 1074 (5); 1101 (1.2; b); 1144 (1; b); 1170 (1.5); 1196 (1.5); 1206 (0); 1237 (1.5); 1268 (2); 1322 (5); 1380 (5); 1440 (2); 1449 (10); 1640 (0.5); 1664 (20).

The presence in the spectrum of a weak frequency of 1640 cm^{-1} points to the presence of traces of an α-olefinic hydrocarbon in 3,4-dimethylhexene-3.

It is noteworthy that whereas for tetramethylethylene (the first member of the series of tetra-substituted olefins) the characteristic frequency is 1676 cm^{-1} [7], the Raman spectrum of the 3,4-dimethylhexene-3 synthesized by us—also a tetra-substituted olefin—contains a frequency of 1664 cm^{-1} i.e., lower than that of tetramethylethylene.

3. Reaction of Crystalline Diisopropenyl Dichloride with Propyl Magnesium Bromide

Reaction of propyl magnesium bromide (123 g propyl bromide, 24 g magnesium and 300 ml absolute ether) with diisopropenyl dichloride (m.p. 35° 47.5 g) was effected in the same conditions as described above for the reaction with methyl magnesium bromide. After two experiments had been carried out, the ether extracts were combined and worked up in the usual manner; the residue was distilled over sodium in a column with 30 theoretical plates. Two fractions were obtained.

The first fraction with b.p. 65-80° (21 g) was a mixture of diisopropenyl and hexane formed by the side reaction of cleavage of chlorine from the dichloride. To remove all of the formed diisopropenyl and separation of the n-hexane in the pure form, the fraction was treated with maleic anhydride and then distilled over sodium in a column of 50 theoretical plates. [illegible] g of hexane (17% of the theoretical calculated on the diisopropenyl dichloride) was isolated. Its constants were:

B.p. 68.5° (750 mm) n_D^{20} 1.3760 d_4^{20} [illegible] Calculated 29.90.

Literature data [6]. B.p. 68.8 (760 mm) n_D^{20} 1.3751, d_4^{20} 0.6592.

The second fraction was 5,6-dimethyldecene-5 (IV) with b.p. 200-202°, yield 12 g (11% of the theoretical). After a second distillation in the same column, the residue was free from traces of halogen and had the following constants:

B.p. 201.1-201.2° (751 mm); n_D^{20} 1.4440; d_4^{20} 0.7796, MR_D 57.45. $C_{12}H_{24}$. Calculated: MR_D 57.15.

5.607 mg substance: 17.840 mg CO_2, 7.311 mg H_2O; 4.200 mg substance: 13.320 mg CO_2, 5.490 mg H_2O. Found %: C 86.86, 86.50; H 14.21, 14.29. $C_{12}H_{24}$. Calculated %: C 85.72; H 14.28.

5,6-Dimethyldecene-5 has not been described in the literature.

The Raman spectrum of 5,6-dimethyldecene-5 contained the following frequencies (intensities evaluated visually).

* The Raman spectra were plotted in the previously described conditions [1,2].

276 (1); 333 (0.8); 397 (0.5); 410 (1); 491 (1); 522 (1); 586 (1.5); 603 (0.5); 671 (0.5); 695 (1.5); 735 (0.5); 750 (1); 792 (1); 821 (2.5); 845 (0.5); 873 (3); 895 (4); 925 (1); 956 (1); 998 (1); 1050 (4); 1058 (1); 1085 (1); 1102 (4); 1123 (0.5); 1170 (0.5); 1198 (1.5); 1241 (1; h); 1290 (1.5); 1301 (2.5); 1329 (1.5); 1382 (3); 1408 (1); 1443 (10; w); 1459 (3); 1640 (1.5); 1665 (12).

Judging by the Raman spectrum, 5,6-dimethyldecene-5 contained about 10% of an α-olefinic hydrocarbon. Formation of the latter may be explained by allylic rearrangement of an intermediate product of reaction—the unsaturated monochloride (see scheme above).

Consequently, in its reaction with propyl magnesium bromide, diisopropenyl dichloride (II) behaves similarly to butadiene 1,4-dichloride, whose reaction with butyl magnesium bromide also leads to formation of an α-olefinic hydrocarbon isomeric with the main reaction product—an alkene with a central double bond [3].

The spectrum of 5,6-dimethyldecene-5, like that of 3,4-dimethylhexene-3, contains a characteristic frequency of 1668 cm^{-1}, whose value is lower than for tetramethylethylene.

SUMMARY

1. Reaction of the crystalline dichloride of diisopropenyl (2,3-dimethylbutadiene-1,3) with methyl magnesium bromide gave 3,4-dimethylhexene-3 in 23% of the theoretical yield, not previously described in the literature; the hydrocarbon has a branched structure and a central double bond. 3,4-Dimethylhexene-3 was characterized by its constants and its Raman spectrum.

2. Reaction of crystalline diisopropenyl dichloride with propyl magnesium bromide gave a mixture of two hydrocarbons (11% yield). 5,6-dimethyldecene-5 (90%) and an isomeric α-olefinic hydrocarbon (10%) formed by allylic rearrangement of an intermediate reaction product—an unsaturated monochloride.

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Chair of Organic Chemistry
Moscow State University

• See Consultants Bureau English translation, page 55.

•• See Consultants Bureau English translation, page 443.

SYNTHESIS OF HYDROCARBONS

XL. REACTION OF CYCLOPENTADIENE DICHLORIDE WITH ORGANOMAGNESIUM COMPOUNDS

R. Ya. Levina, T. I. Tantsyreva and E. G. Treshchova

The reaction of organomagnesium compounds with unsaturated 1,4-dihalides of the allyl type, studied in previous papers by one of us [1-4], was developed as a new method of synthesis of difficultly accessible olefinic hydrocarbons (trans-form) with normal and iso structures and containing a central double bond.

$$ClCH_2-CH=CH-CH_2Cl + 2RMgBr \longrightarrow R-CH_2-CH=CH-CH_2-R$$

(R = CH_3, C_2H_5, C_4H_9)

$$ClCH(CH_3)-CH=CH-CHCl(CH_3) + 2RMgBr \longrightarrow R-CH(CH_3)-CH=CH-CH(CH_3)-R$$

(R = CH_3, C_2H_5)

A similar type of reaction, applied to 1,4-dichlorides of the propargyl type (containing a triple bond), served as a method of synthesis of symmetrical dialkyl acetylenes with normal [5,6] and iso structures [7,8]:

$$ClCH_2-C\equiv C-CH_2Cl + 2RMgBr \longrightarrow R-CH_2-C\equiv C-CH_2-R$$

(R = CH_3, C_2H_5, C_3H_7, C_4H_9)

$$R-CHCl-C\equiv C-CHCl-R + 2CH_3MgBr \longrightarrow R-CH(CH_3)-C\equiv C-CH(CH_3)-R$$

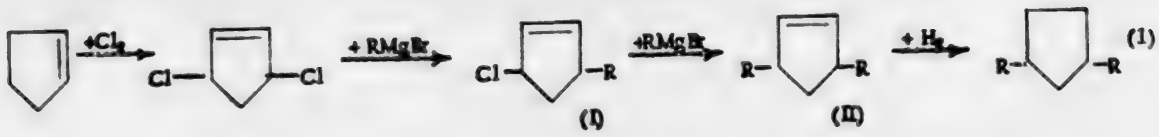
(R = CH_3, C_2H_5, C_3H_7)

Continuing our investigation of the reaction between organomagnesium compounds and unsaturated 1,4-dihalides containing labile halogen atoms, we have extended it to the 1,4-dichloride of cyclopentadiene. In a previous communication [9] we described our preliminary experiments on the reaction of cyclopentadiene dichloride with methyl magnesium bromide. It was established for the first time that the dichloride exchanges each chlorine atom for the radical of the organomagnesium compound to form dimethylcyclopentene (yield 20% of the theoretical).

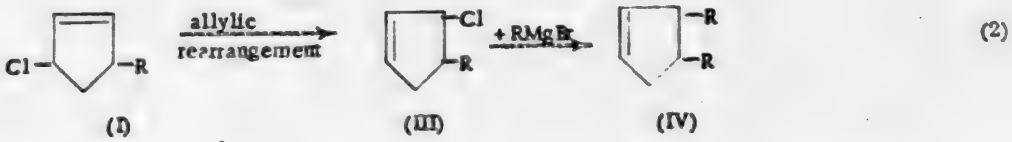
In the last two years two attempts to realize such a reaction with the aim of synthesizing 3,5-dialkylcyclopentenes have been described in the literature. The dibromide of cyclopentadiene was used in both investigations. Reid and Vost [10] in studying this reaction arrived at the conclusion that cis- and trans-3,5-dibromo-cyclopentenes (1,4-dibromides of cyclopentadiene) do not react in the normal way with organomagnesium compounds but form only polymers. In the literature [11] is described a reaction between cis- and trans-3,5-dibromocyclopentadienes and ethyl magnesium bromide; diethylcyclopentene was isolated from the reaction products in a yield of 25% of the theoretical, in the authors' words this compound consisted "partly at least of 3,5-diethylcyclopentene". The reaction of 1,4-dibromocyclopentadiene with octyl magnesium bromide apparently gave a dioctylcyclopentene in which the position of the octyl groups was likewise not established. Consequently the structure of the hydrocarbons formed in these reactions was not conclusively established by the authors.

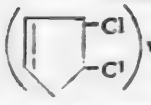
In the present research a close study was made of the reaction between organomagnesium compounds and cyclopentadiene dichloride. Reaction of cyclopentadiene 1,4-dichloride with organomagnesium compounds might serve as a method of synthesis of 3,5-dialkylcyclopentenes-1 (I), hydrogenation of which might yield the difficultly accessible 1,3-dialkylcyclopentanes:*

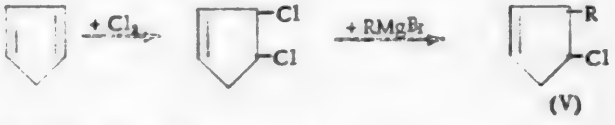
* 3,5-Dialkylcyclopentenes are also interesting because derivatives of one of them — 3,5-disec.butylcyclopentene — are auxins a and b (plant-growth promoters [12]).



Since, however, the intermediately formed monochloride (I) is susceptible to allylic rearrangement to the isomeric monochloride (III), the reaction may also lead to formation of a second hydrocarbon —3,4-dialkyl-cyclopentene-1 (IV):



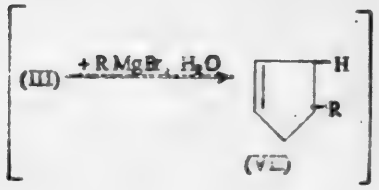
It must also be noted that the starting cyclopentadiene chloride could also contain the 1,2-dichloride  which possesses only one labile chlorine atom. The presence of this dichloride need not interfere with the reaction with the organomagnesium compound because —as we have previously shown [2] —unsaturated 1,2 dichlorides (e g. butadiene 1,2-dichloride), on reaction with organomagnesium compounds, rearrange to 1,4 dichlorides which also enter into further reaction; in that event, even if the 1,2-dichloride should after all remain in the reaction mixture, then one of the reaction products would be the monochloride (V) which does not belong to the allyl chloride series and does not enter into further substitution reaction; for this reason, it should be an easy matter to separate the resultant hydrocarbons (II and IV):



The investigation showed that in the reaction of cyclopentadiene dichloride with methyl magnesium bromide both possible reaction products —3,5-dimethylcyclopentene-1 (II) and 3,4-dimethylcyclopentene-1 (IV) —are formed in a total yield of 20% of the theoretical, as evidence of this reaction course, hydrogenation of this hydrocarbon mixture gave a catalyzate containing (as demonstrated by the Raman spectrum) 1,3-dimethylcyclopentane (in the cis- and trans- forms) (approx. 60-70%) and 1,2-dimethylcyclopentane (trans form) (approx. 40-30%).

Thus, during the reaction, allylic rearrangement does actually take place of the initially formed monochloride (I) (see equation 2).

Study of the reaction between cyclopentadiene dichloride and other organomagnesium compounds (ethyl magnesium bromide and propyl magnesium bromide) showed that with them the reaction likewise proceeds in the same direction, i.e., the intermediately formed monochloride (I) is reduced to 3-alkylcyclopentene-1 (VI) [with possible admixture of 4-alkylcyclopentene-1 (VII)]:



This reaction is a secondary one when using ethyl magnesium bromide [yield of ethylcyclopentene (VI) is 5% and that of the diethylcyclopentenes (II) and (IV) is 12% of the theoretical] but is the sole reaction when using propyl magnesium bromide (the yield of propylcyclopentene is 7% of the theoretical); dipropylcyclopentene is not formed at all. Consequently with increasing size of carbon chain in the radical of the organomagnesium compound, this side reaction becomes predominant. Formation of high-boiling polymers is observed in all the reactions that we studied.

On the basis of the experimental data of this investigation of the reaction between cyclopentadiene dichloride and organomagnesium compounds, the above equations (1-5) may be considered to reflect all possible directions of the reaction.

EXPERIMENTAL

Chlorination of cyclopentadiene. Into a solution of 33 g (0.5 mole) cyclopentadiene * in absolute ether (1:1 by volume) was introduced, with salt-snow cooling, dry chlorine until the weight had increased by 35.5 g (0.5 mole). After distilling off the ether (in vacuum in a nitrogen stream) and fractional distillation of the reaction product in vacuum in a stream of nitrogen (in a tall column), there was obtained 41 g dichlorocyclopentene (yield 60% of the theoretical calculated on the cyclopentadiene):

B.p. 35° (5 mm); 50° (10 mm); n_D^{20} 1.5026 d_4^{20} 1.2193 MR_D 33.20 $C_5H_6Cl_2$. Calculated: MR_D 32.36; EM_D 0.84. Occurrence of an exaltation of the molecular refraction is characteristic of unsaturated 1,4-dichlorides of the allyl type [2,3].

3.885 mg substance: 2.020 mg Cl_2 5.730 mg substance 2.970 mg Cl_2. Found %: Cl 51.99, 51.75. $C_5H_6Cl_2$. Calculated %: Cl 51.76.

Dichlorocyclopentene rapidly darkens in the air and turns yellow even when kept in a sealed ampoule under nitrogen.

* The cyclopentadiene was prepared by depolymerization of the dimer by the method described by S. A. Kazansky and E. M. Terentyev [13]. Technical cyclopentadiene dimer was first washed with concentrated caustic alkali and then with water, dried with calcium chloride and distilled in vacuum (b.p. 70° at 24 mm).

By analogy with the formation of the stereoisomeric 1,4-dibromides on bromination of cyclopentadiene, we may conclude that the dichloride is cyclopentadiene 1,4-dichloride.

In each experiment the dichloride was accompanied by a considerable amount of higher boiling fractions apparently containing cyclopentadiene tetrachlorides. The chlorination of cyclopentadiene has not been described in the literature.

Reaction of cyclopentadiene dichloride with methyl magnesium bromide. To the methyl magnesium bromide prepared from 520 g (5.2 moles) methyl bromide and 96 g magnesium was added with constant stirring and cooling with snow and salt an ethereal solution of 120 g (0.88 mole) freshly distilled (in a nitrogen stream) cyclopentadiene dichloride. After the addition of the whole of the dichloride, stirring was continued for another 3 hours at room temperature and for 4 hours with heating.

Decomposition of the reaction mixture was effected with dilute acetic acid (2 N); the aqueous solution was separated and twice extracted with ether. After working up the ethereal solution in the usual manner and distilling off the ether, the residue was distilled off from polymers boiled in presence of sodium and twice distilled over sodium. The polymer- and halogen compound-free reaction product was distilled over sodium in a column with 50 theoretical plates; a hydrocarbon fraction (dimethylcyclopentenes) was obtained with the following constants:

B. p. 81-82° (751 mm); n_D^{18} 1.4200; d_4^{18} 0.7614; MR_D 31.96. C_7H_{12}. Calculated: MR_D 31.86.

The yield of hydrocarbon was 16 g or 80% of the theoretical calculated on the cyclopentadiene dichloride.

The Raman spectrum of the 81-82° fraction contained a frequency of 1613 cm^{-1}. This showed that the fraction contained a cyclopentene hydrocarbon (or a mixture of cyclopentenes) with alkyl groups not located at the double bond; both 3,5-dimethylcyclopentene-1 (II) and 3,4-dimethylcyclopentene-1 (IV) possess such a structure. Hydrocarbons with this structure are characterized by the presence in the Raman spectrum of the 1612-1619 cm^{-1} lines [14]. Cyclopentene hydrocarbons whose alkyl groups are linked to the double bond carbons are distinguished by the frequency range of approximately 1650-1680 cm^{-1} [14].

3,5- and 3,4-Dimethylcyclopentenes [1] —possible products of the reaction —have not been described in the literature.

The obtained mixture of dimethylcyclopentenes was hydrogenated at 150° over nickel-on-alumina. The catalyzate was distilled over sodium in a column with 25 theoretical plates:

B. p. 89.5-90.5° (756 mm); n_D^{18} 1.4118; d_4^{18} 0.7457; MR_D 32.71. C_7H_{14}. Calculated: MR_D 32.33.

10.380 mg substance: 32.560 mg CO_2; 13.410 mg H_2O. 10.640 mg substance: 33.320 mg CO_2; 13.840 mg H_2O. Found %: C 85.61, 85.46; H 14.46, 14.56. C_7H_{14}. Calculated %: C 85.71; H 14.29.

Literature data for the possible components of the catalyzate: 1,3-dimethylcyclopentane (mixture of isomers) [15] b. p. 89.5-90.6° (760 mm); n_D^{15} 1.4092; d_4^{15} 0.7460; trans-1,2-dimethylcyclopentane [16] b. p. 91.2-91.5° (755 mm); n_D^{25} 1.4210; d_4^{25} 0.7525.

Since it was impossible to fractionate these closely boiling hydrocarbons by distillation in a column, the catalyzate was examined by Raman spectrography.

The spectra of the catalyzate and of the synthetic preparations of 1,3-dimethylcyclopentane (mixture of cis- and trans-isomers) and 1,2-dimethylcyclopentane (trans-isomer) are enumerated in Table 1.

Investigation of the Raman spectrum of the catalyzate and its comparison with the literature data for the spectra of synthetic preparations of 1,3- and 1,2-dimethylcyclopentane showed that the catalyzate contains about 60-70% 1,3-dimethylcyclopentane (in the cis- and trans-forms) and about 40-30% 1,2-dimethylcyclopentane (in the trans-form).** The quantitative composition of the catalyzate was calculated from the intense lines of its spectrum (Table 1): 516, 802 and 828 cm^{-1} which are characteristic of 1,2-dimethylcyclopentane (mixture of the cis- and trans-forms) and from the 769 and 897 cm^{-1} lines

* Apart from the 81-82° fraction, there was isolated a 61-67° fraction (2.5 g) which apparently contained methylcyclopentenes (see equations 4 and 5).

** Judging by the Raman spectrum, the catalyzate did not contain cis-1,2-dimethylcyclopentane.

TABLE 1

Raman Spectra		
Of the catalyzate obtained by halogenation	Of 1,3-dimethylcyclopentane (mixture of cis- and trans-isomers)[15]	Of trans-1,2-dimethylcyclopentane [15]
272 (0.7; w)*; 322 (1); 367 (1); 397 (0.5); 432 (1); 496 (2); 516 (3); 550 (0.5); 592 (0.5); 706 (0.5); 769 (2); 802 (3.5); 829 (5); 844 (0); 897 (3); 956 (2; W); 983 (2); 1025 (1.5; w); 1056 (0); 1079-85 (1.5; w); 1099 (3.5); 1144 (2.5); 1160 (2); 1190 (3); 1258 (0.5); 1292 (1.5); 1315 (1.5); 1345 (2); 1374 (1); 1460 (10; w).	272 (0); 358 (0); 373 (3; w); 409 (0); 426 (3; w); 514 (13); 549 (3); 591 (3; w, W) 726 (0); 803 (13; w); 828 (28); 878 (0); 950 (3); 985 (8); 1021 (3; w); 1041 (3; w); 1085 (3); 1101 (3); 1140 (11); 1152 (11); 1188 (2; w); 1251 (0); 1298 (2; w); 1314 (8); 1346 (5); W); 1457 (40; w).	278 (0; w); 326 (0); 364 (0); 497 (35); 527 (5); 586 (0); 607 (4; w); 721 (0); 766 (27; W); 798 (0); 861 (5); 896 (34); 957 (5; w); 1005 (4); 1022 (5); 1081 (13; w); 1147 (10); 1186 (3; w); 1205 (3; w); 1283 (2); 1303 (2); 1340 (5); 1360 (3); 1457 (40; w, W).

which are characteristic of 1,2-dimethylcyclopentane (trans-form). On the basis of these data it is obvious that the product of reaction between cyclopentadiene dichloride and methyl magnesium bromide comprises two hydrocarbons (see equations 1 and 2); the normal product of reaction is 3,5-dimethylcyclopentene-1 (about 60-70 %) together with 3,4-dimethylcyclopentene-1 (about 40-30%) due to allylic rearrangement of the monochloride (I); hydrogenation of these hydrocarbons also gave a mixture of 1,3- and 1,2-dimethylcyclopentanes.

Reaction of cyclopentadiene dichloride with ethyl magnesium bromide. The reaction between cyclopentadiene dichloride (1.2 moles) and ethyl magnesium bromide and separation of the reaction products were carried out by the above-described method. Distillation of the hydrocarbon fraction (freed from halogen compounds and from polymers) over sodium in a column with 50 theoretical plates gave two fractions: I with b.p. 97° (763 mm) and II with b.p. 140.3° (763 mm). Judging by its constants and analytical data, the second fraction was a mixture of diethylcyclopentenes—3,5-diethylcyclopentene-1 and 3,4-diethylcyclopentene-1 (by analogy with the products of reaction of cyclopentadiene dichloride with methyl magnesium bromide).

B.p. 140.3° (763 mm; n_D^{20} 1.4390, d_4^{20} 0.7922. MR_D 41.24. C_9H_{16}. Calculated: MR_D 41.09.

4.160 mg substance: 13.270 mg CO_2; 4.870 mg H_2O. 4.460 mg substance: 13.900 mg CO_2; 5.070 mg H_2O. Found %: C 87.05, 87.03; H 13.10, 12.72. C_9H_{16}. Calculated %: C 87.04; H 12.96.

The yield was 18 g or 12% of the theoretical calculated on cyclopentadiene dichloride.

Literature data: Of the two possible products of reaction 3,4-diethylcyclopentene-1 (IV) has not been described in the literature, and 3,5-diethylcyclopentene-1 has only been mentioned in a recent paper [11]; the authors give the name of 3,5-diethylcyclopentene to the hydrocarbon that they obtained by reacting ethyl magnesium bromide with the 1,4-dibromide of cyclopentadiene and they report the following constants:

B.p. 141°; n_D^{20} 1.4390; d_4^{20} 0.7921.

There is no doubt that the hydrocarbon of the American authors was not a pure 3,5-diethylcyclopentene but a mixture of isomers, similar to the one that we obtained in the experiment with cyclopentadiene dichloride.

The lower boiling fraction (b.p. 97°), judging by its constants and the analytical data, was 3-ethylcyclopentene-1 (VI) [possibly contaminated with 4-ethylcyclopentene-1 (VII)] formed by a side reaction

* Intensities were measured visually in the ten-ball scale.

(see equation 4): b.p. 97° (763 mm); n_D^{20} 1.4310; d_4^{20} 0.7828. MR_D 31.82. C_7H_{12}. Calculated: MR_D 31.85.

6.750 mg substance: 21.620 mg CO_2; 7.660 mg H_2O. 4.862 mg substance: 15.570 mg CO_2; 5.465 mg H_2O. Found %: C 87.41, 87.39; H 12.70, 12.58. C_7H_{12}. Calculated %: C 87.44; H 12.58.

The yield was 5% of the theoretical, calculated on cyclopentadiene dichloride.

Literature data for 3-ethylcyclopentene-1 [17]: b.p. 96.7-98.8° (760 mm); n_D^{20} 1.4319; d_4^{20} 0.7835.

Optical investigation confirmed that the isolated hydrocarbon was 3-ethylcyclopentene (VI), at least in the main. The Raman spectrum of the prepared ethylcyclopentene contained all the lines found in the spectrum of the synthetic preparation of 3-ethylcyclopentene-1 (prepared by reaction of 3-chlorocyclopentene with ethyl magnesium bromide [17] (Table 2).

Reaction of cyclopentadiene dichloride with propyl magnesium bromide. This reaction led to formation of only 3-propylcyclopentene-1 (V) (possibly contaminated with 4-propylcyclopentene-1), which had the following constants after distillation over sodium in a column with 25 theoretical plates:

B.p. 125° (758 mm); n_D^{20} 1.4370; d_4^{20} 0.7918; MR_D 36.47. C_8H_{14}. Calculated: MR_D 36.48.

3.570 mg substance: 11.415 mg CO_2; 4.020 mg H_2O. 4.690 mg substance: 14.995 mg CO_2; 5.335 mg H_2O. Found %: C 87.26, 87.25; H 12.60, 12.75. C_8H_{14}. Calculated %: C 87.20; H 12.80.

The yield was 7% of the theoretical, calculated on the cyclopentadiene dichloride.

Literature data [18]: b.p. 125.9°; n_D^{20} 1.4359; d_4^{20} 0.7910.

TABLE 2

Raman spectra	
Of ethylcyclopentene prepared in the present investigation	Of synthetic preparation of 3-ethylcyclopentene [17]
295 (1)*; 322 (1.2; w); 392 (3); 470 (2); 489 (1.5); 587 (1; w); 719 (1); 746 (0.3; w); 785 (1.5); 852 (2.5); 880 (0.3); 909 (8); 935 (5); 956 (1); 994 (0.8); 1054 (2; w); (1081 (0.5); 1092 (11); 1101 (1.5); 1117 (1.5); 1170 (2); 1196 (2; w); 1241 (0.5); 1261 (0.3); 1278 (4; w); 1310 (1.5); 1340 (1); 1357 (2); 1357 (2); 1382 (0.5); 1439 (10; w); 1459 (4); 1591 (0.3); 1613 (10)	306 (5; w; d); 322 (5; w; d); 397 (11.5); 473 (9); 493 (7); 590 (5; d); 722 (3; d); 757 (2; d); 787 (3; d); 855 (11); 913 (20); 938 (10); 963 (3); 986 (6.5); 1056 (11); 1090 (23); 1120 (17; w; h); 1173 (45); 1204 (2.5; d); 1263 (3.5); 1285 (5); 1317 (6); 1343 (4); 1361 (12); 1385 (7); 1443 (22.5; w.); 1462 (17); 1617 (35).

* Intensities were determined visually; the intensity of the 1439 cm^{-1} line was assumed to be equal to ten arbitrary units.

The Raman spectrum contained the 1612 cm^{-1} line, characteristic of the non-alkylated double bond in the cyclopentene series of hydrocarbons [14]. Dipropylcyclopentene was not detected among the reaction products; consequently the reaction proceeded in one direction only (according to equation 4) with formation of propylcyclopentene.

SUMMARY

1. A study was made of the reaction between cyclopentadiene dichloride and organomagnesium compounds (methyl, ethyl and propyl magnesium bromides).

2. It was established that reaction of cyclopentadiene 1,4-dichloride with methyl magnesium bromide results in both atoms of halogen being successively replaced by methyl groups with formation of the normal product of reaction — 3,5-dimethylcyclopentene-1, but since the intermediately formed 5-chloro-3-methylcyclopentene (II) partially undergoes allylic rearrangement to 3-chloro-4-methylcyclopentene (III) and the latter also enters into reaction with methyl magnesium bromide, a second hydrocarbon is formed in the shape of 3,4-dimethylcyclopentene-1. The mixture of hydrocarbons is formed in a total of 21% of the theoretical and contains approximately 60-70% of 3,5-dimethylcyclopentene-1 and 40-30% of 3,4-dimethylcyclopentene-1.

3. Reaction of cyclopentadiene 1,4-dichloride with ethyl magnesium bromide gives, apart from a mixture of diethylcyclopentenes (yield 12% of the theoretical) 3-ethylcyclopentene-1 (yield 5% of the theoretical). This hydrocarbon is the product of secondary reduction of an intermediately formed monochloride (I) (5-chloro-3-ethylcyclopentene).

4. Reaction of cyclopentadiene 1,4-dichloride with propyl magnesium bromide did not give dipropylcyclopentenes among the reaction products, the only hydrocarbon to be isolated was 3-propylcyclopentene-1 (7% of the theoretical), formed by the above-mentioned secondary reaction.

Considerable amounts of polymers were observed to be formed in all the reactions investigated.

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* See Consultants Bureau English translation, Page 55.

** See Consultants Bureau English translation, Page [illegible].

*** See Consultants Bureau English translation, Page [illegible].

THE DECOMPOSITION OF TRIMETHYLCROTYLAMMONIUM HYDROXIDE

Ya. M. Slobodin and L. N. Shokhor

Of the methods of obtaining unsaturated hydrocarbons, great interest attaches to the one involving decomposition of completely substituted ammonium bases. There are several statements in the literature (by Chugaev, Demyanov and others) to the effect that decomposition of the bases proceeds without isomerization, so that this method ought to yield "normal" products of reaction. It is clear that this generalization is not without exceptions. For example, in the exhaustive methylation of piperidine the last stage gives a quantitative yield of piperylene instead of the "normal" reaction product—a hydrocarbon with isolated bonds [1].

We have established that decomposition of a pyrrolidine base gives an "anomalous" product with conjugated bonds in place of the anticipated product with isolated or allenic bonds, [2].

The foregoing facts show that decomposition of completely substituted ammonium bases containing an unsaturated radical as one of the substituents leads to formation of compounds with conjugated bonds instead of "normal" compounds with isolated or allenic bonds.

In this investigation we have studied the decomposition of trimethylcrotylammonium hydroxide $CH_3CH=CHCH_2N(CH_3)_3OH$.

In the event of a "normal" course of the decomposition, the final product would by methylallene, whereas an "anomalous" course could lead to either butadiene or dimethylacetylene.

Our experiments showed that the only hydrocarbon formed in the decomposition of trimethylcrotylammonium hyroxide is butadiene.

The starting material for the preparation of trimethylcrotylammonium hydroxide was crotyl alcohol, treatment of which with PCl_3 gave crotyl chloride.

In the Raman spectrum of crotyl chloride the double bond was represented by the 1673 cm^{-1} line. The absence from the spectrum of a line in the 1640 cm^{-1} region shows that our crotyl chloride was substantially free from its allyl isomer—3-chlorobutene-1.

Reaction of crotyl chloride with excess of trimethylamine gave trimethylcrotylammonium chloride. Distillation of the latter with a small excess of 40% aqueous KOH decomposed it with formation of butadiene.

EXPERIMENTAL

Crotyl chloride. 40 g crotyl alcohol prepared by reduction of crotonaldehyde with aluminum isopropylate [3] was mixed with 6 g pyridine and run from a dropping funnel into a flask containing 30 g PCl_3. The contents of the flask were thoroughly stirred while cooling with ice water. After all of the alcohol had been added stirring was continued for another hour at room temperature. The contents of the flask were then poured into cold water. The chloride was extracted with ether. The ether solution was dried with calcium chloride and the ether distilled off to leave 26 g chloride with b.p. 83-84°, n_D^{18} 1.4352.

Raman spectrum. 352 (8), 488 (2), 672 (6), 782 (5), 1077 (3), 1181 (4), 1243 (5), 1314 (4), 1384 (2), 1449 (5), 1673 (10).

Trimethylcrotylammonium chloride. 26 g crotyl chloride was treated, while being cooled, with double the theoretical amount of trimethylamine. The mixture was held at room temperature for 40 hours. The precipitated trimethylcrotylammonium chloride was filtered off, washed several times with absolute ether and dried in vacuum.

0.1448 g substance: 9.70 ml 0.1 N $AgNO_3$. Found %: Cl 23.77. Calculated %: Cl 23.74.

Preparation of the hydrocarbon. Into a flask were charged 15 g trimethylcrotylammonium chloride

and a small excess over the theoretical of 40% KOH solution free from carbonate. The distillation flask was connected to a condenser and the receiver was cooled with ice water. The volatile products not condensing at 0° were trapped in a test tube cooled with dry ice. The ammonium base started to decompose during distillation. Heating was continued until the formation of decomposition products had substantially ceased. The contents of the receiver were acidified with sulfuric acid solution. No insoluble compounds were detected. In the test tube (cooled with dry ice) was a readily mobile liquid which distilled without residue below 0°. Its vapor was passed through a sulfuric acid washer for removal of any trimethylamine, after which it was transferred to a flask containing bromine. A crystalline bromide with m.p. 114° was formed. After crystallization from alcohol the m.p. was 117°. A mixed melting test with butadiene tetrabromide did not give a depression.

SUMMARY

Decomposition of trimethylcrotylammonium hydroxide gives butadiene. Formation of appreciable amounts of the "normal" product —methylallene— was not observed.

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THE ORDER OF ADDITION OF ALCOHOLS TO TRIMETHYLETHYLENE OXIDE

A. A. Petrov, B. V. Gantseva, and O. A. Kiseleva

In previous investigations one of the present authors established the general rule that the order of addition to asymmetrical organic α-oxides of different substances is determined by their acid-base character or by the nature of the catalyst used [1]. In an alkaline medium the addition proceeds exclusively (or almost so) according to the Markovnikov rule [2], whereas in an acid medium isomeric compounds are obtained to a greater or lesser extent. Thus, in the presence of alcoholates, the primary-secondary propylene oxide reacts with alcohols to give primary ethers of propylene glycol, but in presence of acids or boron fluoride a mixture of primary and secondary ethers is formed. The primary-tertiary 1,2-epoxy-2-methylpropane in presence of alcoholates forms primary ethers of isobutylene glycol, and in presence of acids or boron fluoride it gives tertiary ethers of isobutylene glycol. Such an order of addition of alcohols to propylene oxide is confirmed by a series of investigations by foreign authors [3,4]. In precisely the same way there is a sharp difference in the order of addition of alcohols to butadiene oxide depending upon the character of the catalyst [5, 6, 7]; this is also true of other unsaturated oxides, for example styrene oxide [8], 2-methyl-1-butene-3-yne oxide [9], etc. This law, discovered for the reaction of asymmetrical oxides with alcohols, evidently has a general character and may be extended to the reactions of these oxides with other components in particular to hydrogenation reactions [10, 11].

As a further contribution to knowledge in this field it was of undoubted interest to study the order of addition of alcohols to the secondary-tertiary trimethylethylene oxide and to compare it with the order of addition of the same compounds to primary-secondary and primary-tertiary α-oxides.

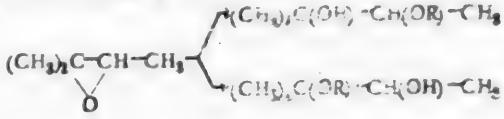
Trimethylethylene oxide is a representative of a class of little investigated substances. It was first prepared by Eltekov [12] by the action of caustic alkali on trimethylethylene chlorohydrin. Studies have been made of the addition to it of water [12], hydrogen halides [13], organometallic compounds [14-16], and ammonia and amines [17-20]. Ammonia and amines (dimethylamine, diethylamine, piperidine and benzylamine), as bases, add on strictly according to the Markovnikov rule. With hydrogen chloride, the reaction proceeds contrary to the Markovnikov rule and the main product is the secondary alcohol.

Of considerable interest is the reaction of trimethylethylene oxide with simple and mixed organometallic compounds. In both cases the reaction proceeds with rupture of the oxide bond at the secondary carbon atom with formation of tertiary alcohols. In this instance, therefore, organomagnesium compounds react like alkaline components.

A. A. Tyazhelova [21] has studied the reaction of trimethylethylene oxide with alcohols in presence of alcoholates. She obtained monoethers of trimethylethylene glycol from ethyl through isoamyl but their structure was not established. Nor was the effect of the nature of the catalyst examined.

Our experiments have shown that trimethylethylene oxide and alcohols give entirely different substances in acid and alkaline media.

Reaction of trimethylethylene oxide with alcohols would be expected to yield secondary or tertiary ethers of trimethylethylene glycol according to the scheme:



Addition of methyl and ethyl alcohols in presence of sodium alcoholate gave exclusively secondary ethers of 2-methylbutanediol [2,3]. The ethyl ether of this glycol, as already noted, was prepared by A. A. Tyazhelova. It is also reported that it can be prepared by the action of methyl magnesium iodide on the ethyl ester of α-ethoxypropionic acid [22], as well as by other methods [23].

With the aim of elucidating the structure of the products of reaction of trimethylethylene oxide with methyl and ethyl alcohols in an alkaline medium, we prepared the anticipated secondary ethers of trimethylethylene glycol by the action of methyl magnesium iodide on the methyl ester of α-methoxypropionic acid and on the ethyl ester of α-ethoxypropionic acid.

The constants of the ethers prepared from trimethylethylene oxide and from the full esters of lactic acid, as set out in Table 1, are seen to be substantially identical. Since the structure of the esters prepared by the latter method is not subject to doubts, it is established that the substances prepared from the oxide are secondary monoethers of trimethylethylene glycol.

TABLE 1

Substance	B. p. °C	d_4^{20}	n_D^{20}	MRD Found	MRD Calcd.	Method of preparation
$(CH_3)_2C(OH)-CH(OCH_3)-CH_3$	131-132.5	0.8963	1.4130	32.88	33.08	From trimethylethylene oxide in presence of alcoholate.
	131-132.5	0.8934	1.4128	32.97	33.08	From methyl ester of methoxypropionic acid.
$(CH_3)_2C(OH)-CH(OC_2H_5)-CH_3$	142-143	0.8756	1.4120	37.59	37.69	From trimethylethylene oxide in presence of alcoholate.
	142-147	0.8754	1.4136	37.68	37.69	Details by A. A. Tyazhelova [21]
	142-143	0.8732	1.4118	37.65	37.69	From ethyl ester of ethoxypropionic acid.
	140-141	–	1.4111	–	–	Details by Stevens for the L-form [23]
$(CH_3)_2C(OCH_3)-CH(OH)-CH_3$	143-144	0.9177	1.4220	32.72	33.08	From trimethylethylene oxide in presence of boron fluoride.
$(CH_3)_2C(OC_2H_5)-CH(OH)-CH_3$	152.5-154	0.8982	1.4208	37.31	37.69	

The tertiary character of the hydroxyl in these substances was confirmed by investigation of their behavior toward acetic anhydride. Acetic anhydride in presence of a drop of sulfuric acid gives the acetates in 50% yield. In the conditions of this reaction, considerable dehydration of the glycol ether takes place with formation of methyl isopropyl ketone.

The constants of the acetates are given in Table 2.

TABLE 2

Compound	B. p. °C	d_4^{20}	n_D^{20}	MRD Found	MRD Calcd.
$(CH_3)_2C(OCOCH_3)-CH(OCH_3)-CH_3$	158-161	0.9460	1.4118	42.12	42.14
$(CH_3)_2C(OCOCH_3)-CH(OC_2H_5)-CH_3$	169-170	0.9243	1.4108	46.78	47.06
$(CH_3)_2C(OCH_3)-CH(OCOCH_3)-CH_3$	168-170	0.9523	1.4140	42.04	42.44

In presence of sulfuric acid or boron fluoride methyl and ethyl alcohols add on to trimethylethylene oxide with formation of monoethers of trimethylethylene glycol markedly different in constants from the already characterized secondary monoethers. Since addition of alcohols to trimethylethylene oxide can only yield two forms of monoethers, we are bound to attribute to the substances formed in presence of acid catalysts the structure of tertiary ethers. This structure was confirmed by their oxidation with chromic acid mixture to the previously described ethers of dimethylacetyl carbinol which were identified by their melting point and the analyses of their semicarbazones.

Due to the fact that these ethers contain a secondary hydroxyl group, they are more easily acetylated by acetic anhydride than are their isomers with a tertiary alcohol group. The acetate of this monoether also differs from the isomer in possessing a pleasanter odor. The constants of the acetates are given in Table 2.

Consequently, this investigation has established that the secondary-tertiary trimethylethylene oxide resembles

the primary-tertiary 1,2-epoxy-2-methylpropane in its behavior toward alcohols in presence of basic and acid catalysts: it forms differing products in alkaline and acidic media.

EXPERIMENTAL

The starting material for this investigation was dimethylethyl carbinol prepared by Grignard synthesis from ethyl bromide and acetone.

Dimethylethyl carbinol was converted into the amylene by slow distillation in a dephlegmator on a water bath over an equal amount of crystalline oxalic acid (the alcohol was added dropwise to the heated acid with continuous distillation). From 150 g carbinol was obtained 86 g trimethylethylene with b.p. 37.5-38.5°. Yield 72%.

Trimethylethylene was converted into the chlorohydrin by the action of a solution of monochlorourea by the method previously described by one of us [13]. From 86 g trimethylethylene was obtained 84 g chlorohydrin (yield 56%) and 5 g water-insoluble products.

The chlorohydrin was converted into the oxide by slow distillation over concentrated KOH solution on the water bath (the chlorohydrin was run dropwise into the heated alkali). From 84 g chlorohydrin was obtained 46.5 g oxide. Yield 79%.

The trimethylethylene oxide with which we worked had the constants: b.p. 73-76°; d_4^{25} 0.8065, n_D^{25} 1.3860. Previously found constants were: b.p. 73-74°; d_4^{25} 0.8038, n_D^{25} 1.3860.

Trimethylethylene oxide was reacted with alcohols in the following conditions.

In 2 moles of the alcohol was dissolved 0.75 g metallic sodium, and to the solution was added 8.6 g (0.1 mole) oxide. The mixture was heated in sealed glass tubes at 100° for 20 hours, after which the tubes were opened and the reaction mixture fractionated in an efficient dephlegmator. The yield of ethers was 45-60%. In one experiment with methyl alcohol when heating was for a total of 6 hours at the boiling point of the alcohol, the yield of ether was negligibly small.

Analytical data for the prepared ethers are set forth in Table 4.

The starting material for the preparation of secondary ethers of trimethylethylene glycol by another method was ethyl bromoacetate.

90 g ester was gradually added through a reflux condenser to a solution of Na alcoholate prepared from 30 g sodium and 200-250 ml methyl or ethyl alcohol. After boiling for 2-3 hours, addition was made to the mixture of water after which it was distilled until the whole of the alcohol had been removed. The mixture was then acidified with 25% sulfuric acid and the alkoxypropionic acid was extracted with ether. The yield of methoxypropionic acid was 68%, that of ethoxypropionic acid 71%.

The constants of the prepared compounds are presented in Table 3 with the literature data.

TABLE 3

Substance	B.p. °C	Pressure (in mm)	$d_4^{t°}$	$n_D^{t°}$	MR_D Found	MR_D Calcd.
$CH_3-CH(OCH_3)-COOH$	87-88	10	1.0915	1.4148	23.87	23.85
ditto [26]	87-89	10	–	–	–	–
$CH_3-CH(OC_2H_5)-COOH$	95	10	1.0875	1.4155	28.54	28.47
ditto [24]	97	11	–	–	–	–
$CH_3-CH(OCH_3)-COOCH_3$	130-131	760	0.9969	1.3968	28.52	28.47
ditto [24]	129.5	752	1.0024	1.3968	28.37	28.47
$CH_3-CH(OC_2H_5)-COOC_2H_5$	153-153.5	760	0.9402	1.4012	37.79	37.71
ditto [24]	155	760	0.9446	1.4012	37.62	37.71

The alkoxypropionic acids were converted into the corresponding esters by saturation of their alcoholic solutions with hydrogen chloride. After standing for 24-48 hours, these solutions were neutralized with sodium carbonate and the reaction products were extracted with ether.

The yield of methyl α-methoxypropionate was 68%, that of the ethyl α-ethoxypropionate was 77.5%. The constants of the esters are presented in Table 3.

Methyl magnesium iodide was reacted with both of the esters in the following conditions. To a solution of CH_3MgI, prepared from 9 g Mg, was added (with mechanical stirring and ice cooling) an ethereal solution of the ester of the alkoxypropionic acid. After standing for a few hours, the reaction mixture was carefully poured into a mixture of ice and a saturated ammonium chloride solution. The ethereal solution was separated. The aqueous solution was again extracted with ether. The ethereal solutions were washed with saturated ammonium chloride solution and then with water and dried over calcined sodium sulfate.

Yield of methyl ester 72%, of ethyl ester 78%. Constants are given in Table 1.

Acetylation of the esters was studied in the following conditions. To a mixture of 4.2 g methyl ester and 5.5 g acetic anhydride (50% excess) was added with cooling a drop of sulfuric acid. Heat was developed after a short period. The reaction mixture was washed with water and with saturated sodium carbonate solution and then distilled. The following fractions were obtained: 1) 90-100°; 2) 109-150°; 3) 155-161°; 4) residue.

With p-nitrophenylhydrazine in acetic acid solution, the first fraction gave the characteristic p-nitrophenylhydrazone of methylisopropyl ketone with m.p. 103-104° (from alcohol).

The third fraction was redistilled. The greater part came over at 158-161° and consisted of the acetate of the alcohol concerned. Yield 50%. The constants appear in Table 2 and the analytical data in Table 4.

Addition of alcohols to trimethylethylene oxide was studied in the following conditions in presence of sulfuric acid. To a solution of 6 g oxide in 75 ml methyl alcohol was added 0.5 ml concentrated sulfuric acid. The temperature rose quickly to 45-50°. After standing for several hours, the sulfuric acid was neutralized with caustic alkali and the mixture distilled through a dephlegmator. In this way about 3 g ether (yield 25%) with the constants listed in Table 1, was obtained.

Treatment of a solution of 8 g oxide in 75 ml methyl alcohol with 0.5 ml boron fluoride etherate caused considerable heat to be developed. The subsequent usual treatment of the mixture gave about 5 g ether. Yield 42%.

In the same conditions the ethyl ether was also obtained in a yield of 42%. A by-product was methylisopropyl ketone.

Oxidation of the tertiary methyl ether of trimethylethylene glycol was performed in the following conditions. To a solution of 2 g of the ether and 0.9 g of sodium bichromate in 25 ml acetic acid (80%) with stirring and cooling (20-25°) was added dropwise a double excess of 25% sulfuric acid. After neutralization of the mixture the oxidation products were extracted with ether. In this way about 1 g of substance distilling at 122-127° and with n_D^{18} 1.4100 was obtained. The constants reported in the literature for dimethylacetyl carbinol [25] are b.p. 124-127° and n_D^{18} 1.4100.

From the products of oxidation was obtained a semicarbazone with m.p. 162° which agrees with the literature data for the methyl ether of dimethylacetylcarbinol semicarbazone.

4.65 mg substance 0.8 ml N_2 (1.5° 759 mm) Found %: N 20.84. $C_6H_{13}O_2N_3$ Calculated %: N 24.26.

From the products of oxidation in the same conditions of the ethyl ether of trimethylethylene glycol was

TABLE 4

Substance	Wt of sample (mg)	CO_2 (mg)	H_2O (mg)	Found %		Calcuated %	
				C	H	C	H
$(CH_3)_2C(OH)-CH(OCH_3)-CH_3$	12.14	27.22	13.18	61.19	12.15	60.98	11.94
$(CH_3)_2C(OH)-CH(OC_2H_5)-CH_3$	10.22	23.78	11.26	63.50	12.33	63.60	12.20
$(CH_3)_2C(OCH_3)-CH(OH)-CH_3$	9.22	20.36	9.72	61.15	11.81	60.98	11.94
$(CH_3)_2C(OC_2H_5)-CH(OH)-CH_3$	17.48	40.78	19.39	63.66	12.42	63.60	12.20
$(CH_3)_2C(OCOCH_3)-CH(OCH_3)-CH_3$	9.12	19.96	8.32	59.72	10.21	59.97	10.07
$(CH_3)_2C(OCOCH_3)-CH(OC_2H_5)-CH_3$	19.15	43.25	18.00	61.64	10.52	62.04	10.41
$(CH_3)_2C(OCH_3)-CH(OCOCH_3)-CH_3$	11.22	25.13	10.41	59.73	10.15	59.97	10.07

obtained a semicarbazone with m.p. 172°, which agrees with the literature data for the semicarbazone of the ethyl ether of the dimethylacetyl carbinol.

Acetylation of the tertiary methyl ether of trimethylethylene glycol was performed in the same conditions as for the isomeric ethers. The yield of acetate was 75%. Constants appear in Table 2 and analytical data in Table 4.

SUMMARY

1. The addition of alcohols to trimethylethylene oxide was investigated in presence of alcoholates, sulfuric acid and boron fluoride.

2. It was established that in presence of alcoholates the addition of alcohols follows the Markovnikov rule and the secondary monoethers of trimethylethylene glycol are formed. The latter were prepared by another method—by the action of methyl magnesium iodide on esters of α-alkoxypropionic acids.

3. In presence of sulfuric acid and boron fluoride the addition of alcohols proceeds with formation of tertiary ethers of trimethylethylene glycol. The structure of the latter was confirmed by oxidation to ethers of dimethylacetyl carbinol which have been described in the literature.

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ALKANE SULFONIC ACIDS

VIII. SYNTHESIS AND PROPERTIES OF ACYLAMIDES OF 2-METHYLETHANE- AND BUTANESULFONIC ACIDS

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We have described acet-, propion- and benzamides of chloromethane-, α-chloromethane-, methane- and ethanesulfonic acids [1]. As already noted, of these derivatives, the benzamides possess an extremely sweet taste (specifically, only the benzamides of alkane- and, in particular, α-chloroalkanesulfonic acids). The benzamides of benzylbenzenesulfonic acids do not possess this property. We thus drew attention to the role of the alkyl and chloroalkyl radicals in imparting a sweet taste to these compounds. This property is induced not only by the alkyl radical but also by its combination with the $SO_2NHCOC_6H_5$ grouping, since acetamides and propionamides with the same alkyl radicals are not sweet.

In the present investigation we prepared and characterized the acet-, propion- and benzamides of 2-methylethane- and butanesulfonic acids. Apart from their preparation, we were interested in the effect of increasing chain length on the sweetness of benzamides. It was found that the benzamide of 2-methylethanesulfonic acid possesses a markedly sweet taste, although weaker than that of the derivatives of chloromethane-, α-chloroethane-, methane- and ethanesulfonic acids. The benzamide of butanesulfonic acid is perfectly tasteless.

The observations made in this investigation permit the conclusion that the sweetness is weakened with increasing chain length and finally disappears. It seems probable that a special function is exercised in respect to this property by methyl and chloromethyl groups directly linked to the benzoylsulfamino grouping. With increasing distance of these radicals from the benzoylsulfamino grouping, the sweetness disappears. The taste of these compounds was only determined organoleptically. The compounds which we prepared are crystalline bodies; the acetamides and propionamides have good solubility in water in the cold, but the benzamides are only soluble when hot. In aqueous solutions they are all weakly acidic (pH 4-5); they readily dissolve in caustic alkalies. The general equation for the reaction is: $RSO_2NH_2 + R'COCl \rightarrow RSO_2NHCOR' + HCl$.

EXPERIMENTAL *

1. Preparation of 2-methylethanesulfonamide. 6.2 g 2-methylethane sulfochloride was dissolved in 50 ml absolute benzene. Into the solution in the course of half an hour was passed a slow stream of dry ammonia at 0°, after which the temperature was raised to 50° and the ammonia was passed in for another half hour. At the end of the reaction the precipitate of ammonium chloride was filtered off. The benzene was distilled off from the benzene filtrate on the water bath and the oily residue was distilled in vacuum. The unreacted sulfochloride came over, leaving in the flask the amide, which solidified on cooling to a greyish-yellow mass. The amide was extracted from the distillation flask and recrystallized from benzene. The filtered ammonium chloride was repeatedly extracted with benzene (using the benzene distilled off from the reaction mixture). On cooling, the extract deposited white crystals of 2-methylethanesulfamide. Total yield of amide 1.5 g or 35% of theory. M. p. 60°.

2. Preparation of butanesulfonamide. 5 g butanesulfochloride was dissolved in 50 ml kerosene. Into the solution was passed a stream of dry ammonia at −5° for 15 minutes. At the conclusion of the reaction, the kerosene was separated and the amide was isolated from the residue (mixture of amide and ammonium chloride) by repeated extraction. Yield 2.25 g or 51% of the theoretical. Slightly yellow crystals, greasy to the touch. m.p. 43-45°.

3. Preparation of the acetamide of 2-methylethanesulfonic acid ** 0.5 g 2-methyl ethanesulfonamide

* V. I. Dubinina and V. A. Malakhov took part in the experimental work.

** Acet- and propionamides were prepared by the same method.

and 0.48 g acetyl chloride were taken. The mixture was refluxed on a boiling water bath for 1½ hours. At the end of the reaction the cooled mixture solidified to a dense grey mass. The product was recrystallized from benzene. M.p. 89°. Yield 0.5 g or 71% of the theoretical. Similar results are obtained by carrying out the reaction with acetic anhydride. 2-Methylethanesulfoacetamide is hygroscopic and has a sour taste.

0.1118 g substance: 6.67 ml 0.1 N H_2SO_4. 0.1506 g substance: 0.2114 g $BaSO_4$. Found %: N 8.35; S 19.24. $C_3H_{11}O_3NS$. Calculated %: N 8.48; S 19.39.

4. Preparation of the acetamide of butanesulfonic acid. 1 g butanesulfonamide and 0.9 g acetyl chloride were taken. Yield of butanesulfoacetamide 1 g or 70% of the theoretical. White platelets, m.p. 68°, sour-astringent taste, hygroscopic.

0.1168 g substance: 6.57 ml 0.1 N H_2SO_4. 0.1032 g substance: 0.1325 g $BaSO_4$. Found %: N 7.87; S 17.66. $C_6H_{15}O_3NS$. Calculated %: N 7.82; S 17.87.

5. Preparation of propionamide of 2-methylethanesulfonic acid. 0.5 g 2-methylethanesulfonamide and 0.45 g propionyl chloride were taken. The crude 2-methylethanesulfopropionamide was recrystallized from a mixture of benzene and gasoline. M.p. 103°. Yield 0.24 g or 35% of the theoretical. Hygroscopic, sour taste.

0.1210 g substance: 6.32 ml 0.1 N H_2SO_4. 0.1012 g substance: 0.1318 g $BaSO_4$. Found %: N 7.31; S 17.32. $C_6H_{15}O_3NS$. Calculated %: N 7.85; S 17.87.

6. Preparation of propionamide of butanesulfonic acid. 1 g butanesulfonamide and 0.8 g propionyl chloride were taken. Yield of butanesulfopropionamide (recrystallized from gasoline-benzene) was 1.1 g or 81% of the theoretical. Colorless plates, m.p. 67°. Sour-astringent taste, hygroscopic.

0.1230 g substance. 6.39 ml 0.1 N H_2SO_4. 0.1640 g substance: 0.1952 g $BaSO_4$. Found %: N 7.27; S 16.31. $C_7H_{15}O_3NS$. Calculated %: N 7.20; S 16.58.

7. Preparation of benzamide of 2-methylethanesulfonic acid. 0.5 g of 2-methylethanesulfonamide and 0.75 g benzoyl chloride were heated on an oil bath at 150–160° under a reflux condenser for 2 hours. The resultant black, viscous oil was transferred to a watch glass for evaporation of the excess of benzoyl chloride. On rubbing with a glass rod while cooling, the viscous oil solidified. The dark-grey 2-methylethanesulfobenzamide was recrystallized from alcohol and water. M.p. 119°. Yield 0.4 g or 55% of the theoretical. Colorless crystals with a slightly sweet taste.

0.1620 g substance: 6.88 ml 0.1 N H_2SO_4. 0.1394 g substance: 0.1444 g $BaSO_4$. Found %: N 5.94; S 14.20. $C_{10}H_{15}O_3NS$. Calculated %: N 6.16; S 14.09.

8. Preparation of benzamide of butanesulfonic acid. 1 g butanesulfonamide and 1.2 g benzoyl chloride were taken. Further procedure as in the preceding experiment. Yield of butanesulfobenzamide 0.6 g or 33.3% of the theoretical. Colorless crystals melting at 65°. Tasteless.

0.1415 g substance: 5.91 ml 0.1 N H_2SO_4. 0.1097 g substance: 0.1033 g $BaSO_4$. Found %: N 5.84; S 12.91. $C_{11}H_{15}O_3NS$. Calculated %: N 5.80; S 13.27.

SUMMARY

1. Acet- propion- and benzamides of 2-methylethane- and butanesulfonic acids were prepared and characterized.

2. It was noted that the acet- and propionamides possess a sour or sour-astringent taste, 2-methylethane sulfobenzamide has a sweet taste, and butanesulfobenzamide is tasteless.

3. It is shown that the sweet taste of the benzamides of alkanesulfonic acids is weakened with increasing length of aliphatic radical chain and finally disappears.

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THE REACTION OF SULFURYL CHLORIDE WITH VINYL CHLORIDE

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It is known that the reaction of carboxylic acid chlorides with acetylene or vinyl chloride in presence of aluminum chloride leads to formation of β-chlorovinyl ketones [1,2,3] whose high reactivity formed the basis of a series of methods of synthesis of heterocyclic and other compounds [4,5,6]. In this connection it seemed of interest to investigate the reaction of chlorides of sulfo acids with acetylene and vinyl chloride in presence of aluminum chloride. For investigation showed that the chlorides of aliphatic and aromatic sulfo acids do not enter into reaction either with acetylene or vinyl chloride in presence of aluminum chloride in the conditions that we had found suitable for condensation of carboxylic acid chlorides [2]. Subsequently we investigated, instead, the behavior of sulfuryl chloride in the same conditions.

When sulfuryl chloride is condensed with acetylene in presence of aluminum chloride in carbon tetrachloride solution, it is almost completely recovered unchanged; only traces are formed of a substance with a pungent odor and lachrymatory action which is apparently β-chlorovinylsulfochloride. Condensation of sulfuryl chloride with vinyl chloride gave a more definite result. The reaction was effected by passing a stream of vinyl chloride into a carbon tetrachloride solution of sulfuryl chloride to which aluminum chloride was gradually added. From the reaction mixture, after hydrolysis was isolated β,β-dichloroethylsulfochloride in 31.5% yield:

$$CH_2=CHCl + SO_2Cl_2 \xrightarrow{AlCl_3} CHCl_2CH_2SO_2Cl.$$

Even after prolonged passage of vinyl chloride in presence of two moles of aluminum chloride, we were unable to detect the formation of β,β,β',β'-tetrachlorodiethylsulfone; this result is fully consistent with the fact that sulfonic acid chlorides, as pointed out above, do not enter into condensation with vinyl chloride. Moreover unlike the reaction of vinyl chloride with carboxylic acid chlorides, which proceeds with cleavage of hydrogen chloride and leads to formation of β-chlorovinyl ketone [3], in our case only addition takes place, and is not accompanied by cleavage of hydrogen chloride.

β,β-Dichloroethylsulfochloride is a heavy colorless liquid with a pungent odor, fairly stable in storage. When it is treated with aqueous-alcoholic caustic alkali, its sulfo group is esterified and one molecule of hydrogen chloride is split off to give the corresponding ester of β-chlorovinylsulfonic acid:

$$Cl_2CHCH_2SO_2Cl + ROH \xrightarrow{NaOH} ClCH=CHSO_2OR;\ R = CH_3,\ C_2H_5.$$

In this way we prepared the methyl and ethyl esters. This route to previously unknown esters of β-chlorovinylsulfonic acids may serve for their preparation. The esters are colorless liquids with a faint odor, stable when kept. Treatment of β,β-dichlorovinylsulfochloride with aqueous caustic alkali gives a substance which behaves like β-chlorovinylsulfochloride. We did not isolate it in the analytically pure form, it was evidently contaminated with the original β,β-dichloroethylsulfochloride.

EXPERIMENTAL

1. β,β-Dichloroethylsulfochloride. Into a solution of 50.0 g sulfuryl chloride in 80.0 ml carbon tetrachloride with stirring and cooling with ice water was passed a vigorous stream of vinyl chloride (prepared from 150 g dichloroethane and a solution of 150 g KOH in 225 ml methanol [7]), and at the same time 60 g $AlCl_3$ was added in the course of an hour. After treatment with the vinyl chloride for 4-5 hours the darkened, homogeneous mass was poured onto ice and stirred for a few minutes. The lower layer was separated, the aqueous layer was extracted with ether; the combined extracts were dried over calcium chloride, the solvent driven off and the residue distilled in vacuum to give a fraction with b.p. 89-92° at 25 mm.

After a second distillation the β,β-dichloroethylsulfochloride had the following constants: b.p. 81-82° at 4 mm; n_D^{16} 1.5066; d_4^{16} 1.6577. Yield 23 g (31.5% of the theoretical). A heavy colorless oil with a pungent odor.

Found %: S 16.20, 16.10. $C_2H_3O_2SCl_3$. Calculated %: S 16.21.

2. Methyl ester of β-chlorovinylsulfonic acid. To a solution of 20 g β,β-dichloroethylsulfochloride in 25 ml methanol was added, with stirring, a solution of 10 g NaOH in 40 ml water at such a speed that the temperature of the mixture was maintained at 0-10°. At the conclusion of the addition of alkali, the mixture was stirred at room temperature for another 30 minutes. The lower layer was then separated and the aqueous layer extracted with ether. The extracts were washed with water and dried over sodium sulfate. The ether was distilled off and the residue distilled in vacuum to give a fraction with b.p. 89-91° at 7 mm. After a second distillation in vacuum, the methyl ester of β-chlorovinylsulfonic acid had the following constants: b.p. 90-91° at 7 mm, n_D^{20} 1.4755; d_4^{20} 1.4244. Yield 6.0 g (38% of the theoretical). Colorless mobile oil with a faint odor, insoluble in water.

Found %: C 23.01, 22.97; H 3.10, 3.17. $C_3H_3O_3SCl$. Calculated %: C 23.19, H 3.22.

3. Ethyl ester of β-chlorovinylsulfonic acid. Prepared by the above procedure from 20.0 g β,β-dichloroethylsulfochloride, 25 ml alcohol and a solution of 10 g NaOH in 40 ml water. Distillation of the reaction product in vacuum gave a fraction with b.p. 103-106° at 10 mm. After a second distillation the ethyl ester of β-chlorovinylsulfonic acid had the following constants: b.p. 96-97° at 7 mm n_D^{20} 1.4688, d_4^{20} 1.3340. Yield 7.0 g (37%). Colorless oil with a faint odor, insoluble in water.

Found %: C 27.68, 27.71; H 4.25, 4.21. $C_4H_5O_3SCl$. Calculated %: C 28.15; H 4.14.

SUMMARY

1. Reaction of sulfuryl chloride with vinyl chloride in presence of aluminum chloride gives β,β-dichloroethylsulfochloride in 31% yield.

2. Treatment of β,β-dichloroethylsulfochloride in solution in an alcohol with aqueous alkali gives the corresponding esters of β-chlorovinylsulfonic acid.

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SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

XXII. THE SULFONATION OF VINYL ETHERS AND ESTERS

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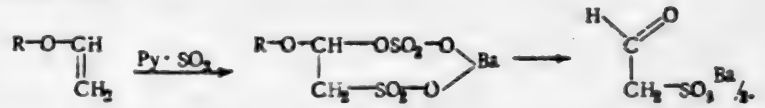
In a previous communication [1] was described the sulfonation of vinylbutyl and vinylisoamyl ethers by the action of pyridinesulfotrioxide in a medium of dichloroethane. This reaction proceeds very slowly at room temperature, but on heating to 60-80° it is completed in 6-8 hours. Hydrolysis of the reaction product in both cases was followed by isolation of a barium salt with the composition $C_2H_3O_4S^{Ba}/_2 \cdot H_2O$, which corresponds to the barium salt of acetaldehyde sulfonic acid. It was shown that an intermediate product is a salt of an alkoxyethionic acid



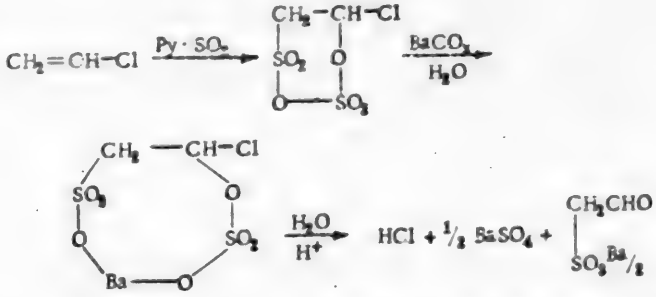
In this investigation we attempted to react pyridine- and dioxane-sulfotrioxides with a whole series of vinyl ethers and esters.

Our first aim was to improve the conditions of sulfonation of vinylbutyl ether with pyridine-sulfotrioxide, since the yield in this reaction did not exceed 30% of the theoretical.

Experiments were carried out on sulfonation in an open vessel (on the water bath under a reflux condenser); attempts were made to sulfonate at lower (30°, 16 days) and higher (150°) temperatures, also without a solvent and in presence of various inert substances. The yields, however, were of the same order (30-35%) since it was still impossible to avoid polymerization completely. We did not isolate any addition products.

Sulfonation was also carried out on vinyl chloride and isocrotyl bromide •, whose structure and properties entitle them to be regarded as vinyl esters of hydrohalogen acids. The literature contains data only for sulfonation (with oleum) of the acid-stable dichloroethylene and trichloroethylene.

In attempts to sulfonate vinyl chloride with sulfur trioxide in dichlorobethane solution we did not observe a reaction at room temperature, while heating to 50-60° resulted in instantaneous polymerization. When heated, however with pyridine-sulfotrioxide in dichloroethane solution (1½-2 hours, 170°), vinyl chloride could be sulfonated. Treatment with barium carbonate and hydrolysis gave a barium salt which analyzed as barium acetaldehydesulfonate.



The greatest difficulty was here encountered in purification from the barium chloride. Silver salts proved to be inapplicable since the silver salt of acetaldehyde sulfonic acid is very poorly soluble. Again, the lead salt was, on the contrary, so hygroscopic that it could not be obtained pure.

• L. L. Obretmova took part in the experimental work.

The problem was solved by extracting the barium chloride with hot ethyl alcohol, and the pure barium salt of acetaldehyde sulfonic acid was obtained free from water of crystallization. The purity and composition of this salt were confirmed by analysis. On recrystallization from water it formed a monohydrate. The yield proved to be very small (5% of the theoretical), and other sulfonation conditions were therefore tried with the aim of avoiding polymerization.

Attempts to sulfonate in ampoules without a solvent or in an ether medium gave even worse resinification. Sulfonation does not proceed at temperatures below 160°. Somewhat better results were got by passing vinyl chloride through a tube with pyridine-sulfotrioxide heated to 160°. In these conditions the yield reached 15%.

As was subsequently established, however, the low yields are due mainly to the large losses during extraction. On analysis of the unpurified salt for barium, sulfur, carbon, hydrogen and halogen, it was found that on the basis of the barium salt it contains only barium acetaldehyde sulfonate in amount corresponding to a yield of 40-50% of the theoretical. In these conditions vinyl bromide is not sulfonated because already at 130° polymerization occurs even in presence of much solvent.

Isocrotyl bromide (prepared by dehydrobromination of isobutylene bromide) sulfonates more readily than vinyl chloride. The reaction begins at only 105° and is complete after 10-15 hours without any substantial polymerization. Yield about 85% (it was not purified from barium bromide).

Turning our attention to vinyl esters, we studied the action of pyridine-sulfotrioxide on vinyl acetate • and isocrotylacetate.

We obtained the best yield of acetaldehyde sulfonic acid by jointly heating the vinyl acetate pyridine-sulfotrioxide and dichloroethane (solvent) in sealed ampoules for 8-10 hours at 110-120°. If the pyridine-sulfotrioxide is taken in equimolar amount then the yield is about 85%. There is no substantial change of yield when using twice the amount of sulfonating agent. The salt obtained by the usual treatment of the reaction product contains, apparently, the barium salt of the sulfonic acid of vinyl acetate $CH_3COOCH{=}CHSO_3^{Ba}/_2$. The presence of this compound is confirmed by the fact that the salt solution decolorizes bromine water and permanganate, and gives off acetic acid when boiled with sulfuric acid, whereas the barium salt of the sulfonic acid of the aldehyde is stable to acids, does not decolorize bromine water and neutral permanganate solution, and turns red when boiled with caustic alkali.

With the aim of effecting smooth removal of the acetic acid, we slightly modified the method of separation of the reaction product in that the sulfonated mass was at once subjected to acid hydrolysis, after which (after distilling off the acetic acid) the treatment with barium acetate was carried out.

$$CH_2{=}CHOCOCH_3 \xrightarrow{Py.SO_3} \begin{matrix} CH_2 & -- & CHOCOCH_3 \\ | & & | \\ SO_2 & & O \\ | & & | \\ O & -- & SO_2 \end{matrix} \xrightarrow[H^+]{H_2O} HOSO_2CH_2CHO + CH_3COOH + H_2SO_4$$

$$HOSO_2CH_2CHO \xrightarrow{BaCO_3} {}^{Ba}/_2\,OSO_2CH_2CHO$$

In a similar manner as for vinyl acetate, sulfonation was effected of isocrotyl acetate (prepared by heating isobutyraldehyde with acetic anhydride and potassium acetate). In this case, however, the reaction proceeds with more difficulty. After 10 hours' heating of isocrotyl acetate with pyridine sulfotrioxide in an ampoule at 150° considerable resinification took place and a portion of the isocrotyl acetate (about 60%) was recovered unchanged. The yield of barium salt of α-isobutyraldehyde sulfonic acid was 35% of the theoretical, calculated on the acetate entering into reaction.

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C{=}CHOCOCH_3 \longrightarrow \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C(SO_3^{Ba}/_2)\text{-}CHO$$

We see from the above that pyridine sulfotrioxide does not in all cases permit of good yields of aldehyde sulfonic acids. On the other hand, sulfonation of aldehydes with dioxane sulfotrioxide gave good results [3].

• E. E. Khaskina took part in the experimental work.

We therefore tried the action of dioxane-sulfotrioxide on some vinyl ethers. Vinylbutyl ether is sulfonated by dioxane-sulfotrioxide even at low temperature with resinification, giving a yield of only 42%. Vinyl acetate does not form resins. The yield of sulfonic acid of the aldehyde (in the form of barium salt) is 62%. In the same conditions isopropenyl acetate gave acetonesulfonic acid in 67% yield.

In the course of our study of the properties of acetaldehyde sulfonic acid, numerous experiments led to the discovery of a derivative possessing a characteristic melting point. This was the S-(β-naphthyl)-thiuronic salt (m.p. 202-204°). Applying the mixed melting point test, we demonstrated the identity between the products of sulfonation of acetaldehyde, [3], vinylbutyl ether and vinylacetate. For the purpose of obtaining a stricter proof of structure, we attempted to replace the chloromercuri-group in chloromercuriacetaldehyde by treatment with sulfur trioxide (chloromercuri)-acetaldehyde was prepared by the method of A. N. Nesmeyanov, N. F. Lutsenko and Z. M. Tumanova by the action of mercuric acetate on vinyl acetate followed by decomposition with sodium chloride [4]. It transpired, however, that in the conditions that we selected, not only substitution of the mercuri-group occurs but also oxidation of the aldehyde group. Consequently the reaction gave the barium salt of sulfoacetic acid. On acidification, this compound readily loses carbon dioxide which turns baryta water cloudy; it does not form an insoluble S-(β-naphthyl)-thiuronic salt

$$ClHgCH_2CHO \xrightarrow{2SO_3} HOSO_2CH_2COOH.$$

Oxidation of acetaldehyde sulfonic acid to sulfoacetic acid has been described previously [1].

On acting on vinyl acetate with dioxane dibromide (proposed for substitution of hydrogen atoms for bromine in vinyl compounds [5]), we obtained — instead of bromovinyl acetate — an addition product, i.e. dibromoethyl acetate. Treatment of this substance with excess of aqueous sodium sulfite solution gave acetaldehyde-sulfonic acid; its S-(β-naphthyl)-thiuronium salt did not give a melting point depression with the previously described specimens

$$CH_2{=}CHOCOCH_3 \xrightarrow{D\cdot Br_2} BrCH_2{-}\underset{\displaystyle Br}{\underset{|}{C}}HOCOCH_3 \xrightarrow[H_2O]{Na_2SO_3} HOSO_2{-}CH_2CHO.$$

As was observed by Schroeter [6] and others [1;3], there is a reduction of the reactivity of the aldehyde group in α-aldehyde sulfonic acids. Nevertheless it was of interest to attempt the cyanohydrin synthesis with the aim, for instance, of obtaining cysteic acid from acetaldehyde-sulfonic acid.

$$\begin{array}{l} CH_2{-}CHO \\ | \\ SO_3H \end{array} \xrightarrow{NH_3 + HCN} \begin{array}{l} CH_2{-}CHCN \\ | \quad\quad | \\ SO_3H \quad NH_2 \end{array} \xrightarrow{H_2O} \begin{array}{l} CH_2{-}CHCOOH \\ | \quad\quad | \\ SO_3H \quad NH_2 \end{array}$$

We carried out a series of experiments with barium, sodium and ammonium salts of acetaldehyde sulfonic acid. The cyanohydrin synthesis was performed by the three main methods described in the literature: Strecker's method (with hydrocyanic acid and ammonia), Lyubavin's method (with ammonium cyanide) and Zelinsky's method (with potassium cyanide and ammonium chloride). The temperature regime was also varied from room temperature to 100°. Different hydrolyzing agents were also tried out: barium hydroxide, sulfuric and hydrochloric acids. The amino acid was determined qualitatively by the ninhydrin reaction and then quantitatively by the Van Slyke and Kjeldahl methods. We did not isolate the substance in the pure state.

It transpired that the barium salt of acetaldehyde sulfonic acid does not react with ammonium cyanide to any substantial extent even at 100° (negative or feeble reaction with ninhydrin). With ammonium cyanide the sodium salt only gives traces of amino acid (5 hours at 35°), but in Zelinsky's conditions (potassium cyanide and ammonium chloride at room temperature) it gives cysteic acid in 12.9% yield. The ammonium salt was tested out in Strecker's conditions and gave yields of 1 to 3%.

Consequently the best conditions for the cyanohydrin synthesis were those of Zelinsky; but even then the yield was low (12.9%). Determination of total nitrogen gave a similar figure (11.4%) which is within the limits of experimental error. Hence the low yield is not due to the reaction proceeding in the direction of formation of amino compounds. To confirm this, we titrated the unreacted cyanogen ion and found that only 15% of the cyanide had been consumed. The low yield is also explained by this fact. An attempt to raise the reaction temperature led to darkening of the mixture and a lowering of the yield.

It has thus been shown that it is possible in principle to perform the cyanohydrin synthesis with α-aldehyde sulfonic acids, the reaction, however, proceeds very sluggishly.

EXPERIMENTAL

Sulfonation of vinyl chloride. A mixture of 5 g (0.02 mole) 25% solution of vinyl chloride in dichloroethane and 6 g (about 0.04 mole) pyridine-sulfotrioxide was sealed into an ampoule and heated for $1^1/_2$-2 hours at 170°. The dark-brown reaction product was dissolved in water, treated with barium carbonate until neutral to Congo and then steam-distilled to remove the pyridine. The residue was filtered; the filtrate was decolorized by boiling with animal charcoal and then evaporated to a small volume; the barium salt was brought down with methyl alcohol. The solid salt was extracted with hot ethyl alcohol for 3 days (in a Soxhlet). The residue was 0.2 g barium acetaldehyde sulfonate, i.e. 5% of the theoretical yield.

8.03 mg substance: 4.918 mg $BaSO_4$. Found %: Ba 36.04. $C_2H_3O_4S^{Ba}/_2$. Calculated %: Ba 35.81.

Sulfonation of isocrotyl bromide. 0.8 g (0.006 mole) isocrotyl bromide and 4.0 g (0.025 mole) pyridine-sulfotrioxide were heated in a sealed ampoule for 6 hours at 110°. After treatment of the reaction product with barium carbonate, distilling off the pyridine, and precipitating with alcohol, there was obtained 1.8 g dry barium salt containing (on the basis of the halogen analysis) about 0.76 g barium bromide. The yield of barium salt of α-isobutyraldehyde sulfonic acid was about 85% of the theoretical. (The compound was not isolated in the pure form). The solution of the salt reduces ammoniacal silver solution and gives a coloration with fuchsine-sulfurous acid. The lead salt was obtained in the form of a thick, syrupy mass containing traces of bromine ion. The silver salt is insoluble in water.

Sulfonation of vinylbutyl ether. a) 2.0 g (0.02 mole) vinylbutyl ether, 3.2 g (0.02 mole) pyridine-sulfotrioxide and 6 ml dichloroethane were heated in a sealed ampoule for 9 hours at 70-90°. The dark mass was converted into barium acetaldehyde sulfonate by boiling on the water bath with an aqueous suspension of barium carbonate until the pyridine had gone off. The precipitate was filtered off and washed with hot water; the filtrate was evaporated to a small volume and the salt brought down by adding methyl alcohol. Yield 2.6 g or 30% of the theoretical.

7.907 mg substance: 5.415 mg $BaSO_4$. 7.832 mg substance: 4.763 mg $BaSO_4$. Found %: Ba 35.79, 35.92. $C_2H_3O_4S^{Ba}/_2$. Calculated %: Ba 35.81.

If the salt is prepared by evaporating the aqueous solution, the barium salt is obtained with one molecule of water of crystallization.

0.0970 g substance: 4.82 ml 0.09982 N Na_2CO_3. 0.0920 g substance: 4.58 ml 0.09988 N Na_2CO_3. Found %: Ba 34.10, 34.15. $C_2H_3O_4S^{Ba}/_2 \cdot H_2O$. Calculated %: Ba 34.34.

b) A mixture of 4.0 g (0.04 mole) vinylbutyl ether, 13 g (0.08 mole) pyridine sulfotrioxide and 40 ml dichloroethane was refluxed in a round-bottomed flask for 14 hours on a water bath. The sulfonated mass was worked up as in the preceding experiment. Yield of barium acetaldehyde sulfonate 5.6 g or 32.5% of the theoretical.

c) A solution of 4.0 g (0.05 mole) sulfur trioxide in 25 ml dichloroethane was cooled to 0°, to it was added 4.4 g (0.1 mole) dioxane, and to the resultant solution of dioxane-sulfotrioxide was added 2.5 g (0.025 mole) vinylbutyl ether. The mixture was left for 6 hours and then decomposed with water and evaporated on the water bath for 4 hours for removal of solvent and butyl alcohol. The residue was treated with barium carbonate and the filtrate evaporated, and barium acetaldehyde sulfonate precipitated by adding methyl alcohol. Yield 2.0 g (42% of theory).

Preparation of S-β-naphthyl thiuronic salt of acetaldehyde sulfonic acid. To a cooled saturated solution of S-β-naphthyl thiuronyl chloride was added a saturated aqueous solution of the barium salt of sulfo-acetaldehyde. A flocculent precipitate formed immediately and was filtered off, dried in vacuum over phosphorus pentoxide and recrystallized from absolute benzene. Colorless crystals with m.p. 202-204°.

Sulfonation of vinyl acetate.

a) A mixture of 2.3 g (0.03 mole) vinyl acetate (b.p. 72-74° at 760 mm; n_D^{19} 1.3958), 5.0 g (0.03 mole) pyridine sulfotrioxide and 10 ml dichloroethane was heated in an ampoule for 8 hours at 120°. The sulfonated mass was dissolved in hot water, 0.5 ml 0.2 N sulfuric acid was added before boiling for 4 hours, the acetic acid was distilled off in steam. The residue was treated with barium carbonate and the pyridine distilled off in steam. The precipitate was filtered and washed with hot water. The filtrate was evaporated down and the barium

acetaldehydesulfonate was precipitated by addition of methyl alcohol. Yield 4.4 g or 85% of the theoretical.

0.0962 g substance: 5.07 ml 0.09988 N Na_2CO_3. 0.0990 g substance: 5.40 ml 0.09988 N Na_2CO_3. Found %: Ba 36.15, 36.21. $C_2H_3O_4S^{Ba}/_2$. Calculated %: Ba 35.81.

b) A solution of 8 g (0.1 mole) sulfur trioxide in 50 ml dichloroethane was cooled to 0°, 8.8 g (0.2 mole) dioxane was added, followed (with stirring) by 4.3 g (0.05 mole) vinyl acetate. The mixture was left for 6 hours, poured into cold water and evaporated for 8 hours on the water bath with two additions of 5 ml water each. The mass was then treated with excess barium carbonate, the precipitate filtered off, and the filtrate evaporated until crystallization started. Cooling brought down 6.5 g of the barium acetaldehyde sulfonate containing one molecule of water of crystallization. Yield 62% of the theoretical. The S-(β-naphthyl)-thiuronic salt had m.p. 202-204°. No depression of m.p. in mixed melting test with the salt prepared from vinylbutyl ether.

Sulfonation of isopropenyl acetate. To an ice-cooled solution of 1.0 g (0.013 mole) sulfur trioxide in 6 ml dichloroethane was added, with stirring, 0.9 g (0.01 mole) dioxane, followed by 1.0 g (0.01 mole) isopropenyl acetate. Working-up in the usual manner gave 1.5 g of the monohydrate of the barium salt of acetonesulfonic acid. Yield 67% of the theoretical.

0.0579 g substance: 0.0306 g $BaSO_4$. 0.0177 g substance: 0.0093 g $BaSO_4$. Found %: Ba 31.05, 30.80. $C_3H_5O_4S^{Ba}/_2 \cdot H_2O$. Calculated %: Ba 30.66.

Preparation of isocrotyl acetate. A mixture of 28.8 g (0.4 mole) isobutyraldehyde, 61 g (0.6 mole) distilled acetic anhydride and 6 g (0.06 mole) potassium acetate was heated for 10 hours on an oil bath under a condenser. The mass was then poured on to ice and the separated layer was washed with ice water and with sodium bicarbonate solution. After drying over magnesium sulfate, the substance was distilled in a dephlegmator, giving 36.5 g isocrotyl acetate or 80% of the theoretical yield. B.p. 121-124° at 756 mm; n_D^{20} 1.4106 in agreement with the literature.

Sulfonation of isocrotyl acetate. 3 g (about 0.025 mole) isocrotyl acetate and 8 g (0.05 mole) pyridine-sulfotrioxide were sealed into an ampoule and heated for 10 hours at 150°. From the thick, partly polymerized mass was distilled off 2.0 g nonreacted isocrotyl acetate. The residue was treated with barium carbonate, the pyridine distilled off in steam. The usual method of working-up gave 0.59 g barium salt of α-isobutyraldehyde sulfonic acid, i.e. 35 % of the theoretical yield, calculated on the isocrotyl acetate entering into reaction.

5.615 mg substance. 3.044 mg $BaSO_4$. 4.331 mg substance: 2.338 mg $BaSO_4$. Found %: Ba 31.90, 31.78. $C_4H_7O_4S^{Ba}/_2$. Calculated %: Ba 31.25.

Action of sulfur trioxide on (chloromercuri)acetaldehyde. In a small flask fitted with a reflux condenser was placed 1.4 g (0.005 mole) (chloromercuri)-acetaldehyde [4], and a solution of 2.0 g (0.025 mole) sulfur trioxide in 30 ml dichloroethane was run in with cooling. The mixture was then heated for 12 hours on the water bath. 10 ml water was added, the dichloroethane was evaporated off on the water bath and the mercury salts were precipitated with hydrogen sulfide. The filtered solution was treated with barium carbonate, filtered, washed three times with boiling water and again evaporated. The poorly soluble salt of sulfoacetic acid was recrystallized from water. Yield 0.6 g (41% of theory) of the monohydrate of the barium salt of sulfoacetic acid.

0.0094 g substance: 0.0075 g $BaSO_4$. Found %: Ba 46.45. $C_2H_2O_5SBa \cdot H_2O$. Calculated %: Ba 46.79.

Reaction of dioxane dibromide with vinyl acetate. To 21.2 g (0.25 mole) vinyl acetate was added, in small portions with cooling, 62 g (0.25 mole) dioxane dibromide [5]. Each portion of the dioxane dibromide quickly dissolved on addition imparting to the reaction mixture the characteristic color of bromine which quickly disappeared however (in 1-2 minutes). After the end of the reaction, the layers were separated. The lower layer was washed with ice water, dried with calcium chloride and distilled in vacuum to give 31.2 g dibromide (50% of the theoretical). Dibromoethyl acetate is a colorless oil with a strong odor of radish. It is lachrymatory. B.p. 101-103°, at 32 mm; n_D^{20} 1.5057 d_4^{20} 1.9170; MR_D 38.24, calculated 37.85.

Literature data: b.p. 84-85° at 5 mm; n_D^{20} 1.5052; d_4^{20} 1.9185 [7].

8.260 mg substance. 5.955 mg CO_2. 1.820 mg H_2O; 5.365 mg Br_2. Found %: C 19.67; H 2.47; Br 64.95. $C_4H_6O_2Br_2$ Calculated %: C 19.54; H 2.46; Br 64.98.

Reaction of dibromoethyl acetate with sodium sulfite. To a solution of 3.0 g (0.025 mole) pure sodium sulfite in 25 ml water was added 2.5 g (0.01 mole) dibromoethyl acetate and the mixture was heated under a reflux condenser. After an hour the mixture had become homogeneous. The light-yellow solution was evaporated, treated with barium carbonate, filtered and again evaporated. The cooled concentrated solution of barium acetaldehyde sulfonate was added to a cooled saturated solution of S-(β-naphthyl)-thiuron chloride. The immediately formed precipitate was filtered, washed with water, dried in a vacuum-desiccator and recrystallized from absolute benzene. M.p. 202-203°. A mixed melting test with the S-(β-naphthyl)thiuronic salt of acetaldehydesulfonic acid prepared from vinyl acetate or from acetaldehyde [3] did not give a depression.

Cyanohydrin synthesis with acetaldehyde sulfonic acid. a) A mixture of 1.0 g (0.005 mole) barium salt of acetaldehyde sulfonic acid and 10 ml (0.007 mole) 3.15% aqueous solution of ammonium cyanide [8] was heated in a sealed ampoule for 5 hours at 60° and then stood for two days at room temperature. Addition was then made of 7 ml concentrated sulfuric acid; the mixture was refluxed for 12 hours, neutralized hot with barium carbonate and filtered. The precipitate was washed with hot water and the combined filtrates were evaporated down on a water bath. The residue gave a weak positive ninhydrin reaction.

b) To a solution (2 ml) of ammonium acetaldehyde sulfonate (prepared from 1.0 g barium salt by treatment with ammonium sulfate) was added 0.3 ml anhydrous hydrocyanic acid. The mixture was stood for 24 hours at room temperature. Then a stream of ammonia was passed through it with ice cooling for an hour, the mass was again left for 24 hours. The reaction mixture was then hydrolyzed with hydrochloric acid and worked up as in the preceding experiment. The ninhydrin test was positive. Van Slyke ammonia determination: 2 ml substance: 0.33 ml N_2 (20° 742 mm). Total amount of solution 23 ml. Yield of amino acid (calculated on the aldehyde) 3.02%.

c) To a mixture of 0.75 g (0.005 mole) sodium acetaldehyde sulfonate, 0.3 g (0.057 mole) ammonium chloride and 0.4 g (0.057 mole) 92% KCN was added a few drops of water and the mass kept at room temperature for 48 hours with periodic shaking. Addition was then made of an equal amount of concentrated acid and the mixture stood for 12 hours at room temperature, diluted with double the amount of water and refluxed for 7 hours. The hydrolyzate was then evaporated to dryness on the water bath. To the dry residue was added a concentrated solution of sodium hydroxide and the ammonia was distilled off. The liquid was then transferred to a measuring flask, made up to the mark and analyzed for nitrogen content.

The yield of amino nitrogen was found to be 12.4% calculated on the aldehyde and 11.4% on the basis of nitrogen volume, which is within the limits of analytical error.

SUMMARY

1. Reaction of sulfur trioxide in complex form (pyridine-sulfotrioxide or dioxane-sulfotrioxide) with vinyl chloride, isocetyl bromide, vinylbutyl ether, vinyl acetate, isopropenyl acetate, and isooctyl acetate gave the corresponding α-aldehyde sulfonic acids or α-sulfoketones, as was established by analyses and by other syntheses of acetaldehyde sulfonic acid.

2. Reaction of (chloromercuri) acetaldehyde with sulfur trioxide leads to substitution of the mercuric group by the sulfo group with simultaneous oxidation to sulfoacetic acid.

3. In the reaction of dioxane-sulfotrioxide with vinyl acetate the hydrogen atom is not substituted but instead a molecule of bromine adds on at the double carbon-carbon bond.

4. Heating of α,β-dibromoethyl acetate with an aqueous solution of sodium sulfite converts it into acetaldehyde sulfonic acid.

5. The possibility of preparing α-amino-β-sulfo acids by the cyanohydrin synthesis from α-aldehyde sulfonic acids is demonstrated.

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SYNTHESES WITH ACRYLONITRILE

XIX. REDUCTION OF ACRYLONITRILE BY VYSHNEGRADSKY'S METHOD

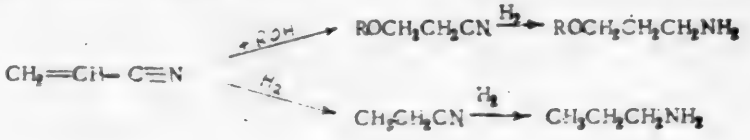
V. G. Yashunsky, A. N. Kost, and A. P. Terentyev

A. N. Kost and V. G. Yashunsky have previously shown [1] that in the reduction of β-substituted propionitriles ($R{-}X{-}CH_2CH_2CN$) with sodium in alcohol, the R–X group is replaced by the alkoxy group of the alcohol in which the reduction is carried out. A mechanism was proposed for this reaction which involved intermediate formation of acrylonitrile and its addition to the alcohol to form the β-alkoxy-propionitrile which underwent reduction to the γ-alkoxypropylamines.

For the purpose of establishing the above mechanism of anomalous reduction of β-substituted propionitriles we carried out the reduction of acrylonitrile itself. The literature only contains details of its catalytic hydrogenation [2]. It has also been shown [3] that acrylonitrile is converted into adiponitrile by the action of magnesium amalgam in a methyl alcohol medium. We reduced acrylonitrile with sodium in ethyl, butyl, isobutyl and isoamyl alcohols. The main products that we isolated were, as anticipated, the corresponding γ-alkoxypropylamines. The lowest yield of alkoxyamine was obtained with ethyl alcohol (30% calculated on the acrylonitrile); reduction in butyl alcohol gave 44.3% of amine, and in isoamyl alcohol 41.4%. The yield of alkoxyamines is considerably increased by working with large quantities (1½ times more than usual) of sodium and alcohol; thus, γ-butoxypropylamine and γ-isobutoxypropylamine were obtained in yields of 59.6 and 63% respectively. Moreover, it was found that increased yields of alkoxyamine can be achieved by running the alcoholic solution of acrylonitrile into the sodium under toluene.

All the reductions of acrylonitrile gave small amounts (up to 13% calculated on the acrylonitrile) of propylamines which were isolated as the hydrochlorides. We have published a short communication on these experiments [4].

The preferential formation of γ-alkoxypropylamines is explained by the fact that in these conditions the most active portion of the acrylonitrile molecule is the double carbon-carbon bond, and therefore competition arises between the reaction of alcohol addition and the reaction of hydrogen addition.



In our conditions the velocity of the first reaction predominates considerably. The large amount of alcohol in which the reduction took place (molar ratio of acrylonitrile to alcohol = 1:45) also promoted the first reaction. The meager literature data about the reduction of nitriles of unsaturated acids by Vyshnegradsky's method indicate that if the double bond is remote from the nitrile group, then reduction leads to the corresponding unsaturated amine [5]. But when the nitrile group is directly located at the double bond, then the latter is hydrogenated with formation of the saturated base although yields of amines rarely reach 20% [6, 7] and, indeed, in the majority of cases only traces of amines can be isolated. The main products of reduction of such nitriles are hydrocarbons. Thus, Freund [6] reduced α-phenylcinnamonitrile and isolated δ, γ-diphenylpropylamine and dibenzyl; the amount of the latter was more than 4 times greater than that of the amine. In the case of cinnamonitrile not even traces of γ-phenylpropylamine could be detected in the end products.

Consequently, if the nitrile group is conjugated with the double bond, then in the conditions of Vyshnegradsky's reaction the reduction of this double bond is inhibited. The result of this is that other reactions can proceed which are facilitated by the presence of the polar CN group.

In our case such a reaction was the addition of an alcohol. In the case of nitriles of cinnamic acids, the formation of alkoxynitriles is evidently hindered by the presence in the β-position of a phenyl radical, and here the reactions proceed in another direction (in the main with cleavage of the nitrile group).

The formation of γ-alkoxypropylamines as the main products of reduction of acrylonitrile by sodium in alcohols is consequently accounted for by the peculiarity of the structure of this molecule which permits reciprocal influence between the CN group and the carbon-carbon double bond.

The preparation of γ-alkoxypropylamines by reduction of acrylonitrile (Vyshnegradsky's method) proved to be a convenient preparative method. For example, for the synthesis of γ-ethoxypropylamine, Utermohlen [8] first performed cyanoethylation of ethyl alcohol (yield 78%) and then catalytic hydrogenation of the obtained nitrile (yield 50%), i.e. the total yield of amine (calculated on the acrylonitrile) was 39%. In the case of γ-butoxypropylamine it was 61%. In our procedure the amine yields are of a similar order but the final products are obtained in one step without separation of intermediate products.

EXPERIMENTAL

Preparation of γ-Ethoxypropylamine

To a boiling solution of 5.3 g (0.1 mole) acrylonitrile in 130 ml absolute alcohol, placed in a two-necked liter flask fitted with a high-capacity reflux condenser, was added 15 g sodium over a period of 20 minutes. After the metal had gone into solution, addition was made to the alcoholic solution of about 100 ml water, and the mixture was steam-distilled for many hours. The distillate was collected in a receiver containing 10% hydrochloric acid. A purer product was obtained by bubbling steam through the hydrochloric acid solution and then evaporating this solution on the water bath. The residue – a thick, yellow oil – was decomposed with solid NaOH under a layer of ether and repeatedly extracted with absolute ether. The ethereal solution was dried with fused KOH, the ether was distilled off, and the base twice distilled in vacuum.

There was obtained 3.0 g γ-ethoxypropylamine (yield 30% calculated on the acrylonitrile). B.p. 49-50° at 30 mm.

Preparation of γ-Isobutoxypropylamine

Into 50 ml hot toluene containing 22 g sodium * was run a solution 5.3 g (0.1 mole) acrylonitrile in 350 ml absolute isobutyl alcohol over a period of 30 minutes. Throughout the whole of the reaction period the flask was heated on an oil bath at a temperature of 140-150°. After the whole of the sodium had dissolved, 200 ml water was added and the mixture distilled with steam. The distillate was collected in dilute hydrochloric acid after checking that the solution was acid to Congo, the alcoholic layer was separated and the isobutyl alcohol distilled off with steam. The residue from the distillation was combined with the aqueous layer from the first distillate and evaporated on the water bath. The γ-isobutoxypropylamine hydrochloride was decomposed with powdered NaOH under a layer of ether; the base was extracted with ether, and the ethereal solution (about 300 ml) was dried with fused KOH. The ether was distilled into dilute hydrochloric acid and the residue distilled in a dephlegmator at reduced pressure. A fraction boiling at 72-73° (34 mm) was collected. Yield 8.27 g or 63.1% of theory calculated on the acrylonitrile. The aqueous layer was separated from the ether distilled into hydrochloric acid and evaporated down on the water bath to give 1.28 g white crystals of propylamine hydrochloride. M.p. (from aqueous alcohol) 166°. The literature [9] gives m.p. 157-158°.

Reduction by a similar method of acrylonitrile in n-butyl alcohol (5.3 g acrylonitrile, 15 g sodium and 220 ml of the alcohol) gave γ-butoxypropylamine in 44.2% yield. B.p. 78-79° at 23mm. On using the same quantities of sodium and alcohol for reduction of 3.2 g (0.060 mole) acrylonitrile, the yield could be increased to 59.6%, b.p. 71-72° at 19 mm.

γ-Isoamyloxypropylamine was isolated from the products of reduction of acrylonitrile with sodium in isoamyl alcohol. Yield 41.4%, b.p. 78.5-80° at 16 mm.

The properties and constants of the alkoxypropylamines obtained by reduction of acrylonitrile correspond entirely to the properties and constants of the amines prepared previously by us [1]. The mixed melting points of the picrates were not depressed.

* The amounts of sodium and alcohol used were 1 1/2 times as much as those usually taken for the reduction process.

SUMMARY

1. For the first time the reduction of acrylonitrile was effected by Bruylants's method (sodium in various alcohols).

2. It was shown that in this reaction the alcohol undergoes cyanoethylation and this is followed by reduction of the nitrile group. The main product of the reaction in 30-60% yield is γ-alkoxypropylamine; only an insignificant amount of isopropylamine is formed.

3. The method can serve as a preparative method for γ-alkoxypropylamines.

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THE REACTION OF ALDEHYDES AND KETONES WITH ACETIC ANHYDRIDE

III. REACTION OF CYCLOPENTANONE, ACETONE AND METHYLPROPYL KETONE WITH ACETIC ANHYDRIDE

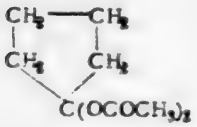
I. V. Machinskaya, V. A. Barkhash and V. I. Molchanov

In previous communications one of us showed that cyclohexanone [1] and its homologs [2] react with acetic anhydride in presence of small amounts of concentrated sulfuric acid at room temperature to form enol acetates; in short-period reaction the enol acetates are accompanied by diacetates of hydrated forms of the ketones.

In this paper we describe the reaction with acetic anhydride, in the same conditions, of cyclopentanone and of some aliphatic ketones.

Cyclopentanone was reacted with acetic anhydride in the same conditions as for cyclohexanone [1].

The data show that cyclopentanone appears to react with acetic anhydride with formation of the enol-acetate, as evidenced by decolorization of bromine water; the enol acetate, however, appears to be unstable and during distillation it partly undergoes cleavage with formation of the original ketone (the distilled fractions always gave a precipitate with bisulfite and had a strong acid reaction to litmus)*. Of the expected reaction products we only succeeded in isolating the previously undescribed diacetate of the hydrate form of cyclopentanone (I), a crystalline product with m.p. 37-39°.



(I)

On comparing our previous results for the reaction of cyclohexanone [1] and its homologs [2] with acetic anhydride with the present results for cyclopentanone, we can conclude that the formation of the acetate of the enol form proceeds more readily in the case of cyclohexanone and its homologs. This conclusion is in harmony with the data of Mousseron and Winternitz [4], of Wallach [5] and of certain other investigators who drew attention to the great tendency to double-bond formation in the cyclohexanone ring in comparison with the cyclopentanone ring.** Mousseron and Winternitz [4] arrived at this conclusion on the basis of stereochemical considerations and of a series of experimental facts. Wallach [5] established that the reaction of acetone with cyclohexanone and its homologs in presence of sodium alcoholate leads to formation of condensation products with a double bond in the ring, whereas with cyclopentanone the condensation products contain a hemicyclic double bond.

We used acetone and methylpropyl ketone in this investigation as representatives of aliphatic ketones.

Previous attempts to prepare the enol acetate by reaction of acetone with acetic anhydride had been made by Mannich [6] and Hancu [7]. In both cases, however, negative results were obtained***; mesityl oxide was isolated from the reaction mixture. Formation of mesityl oxide was also observed [9] when acetone was heated with acetic anhydride in presence of p-toluenesulfonic acid.

We have established that the reaction of acetone with acetic anhydride at room temperature in presence of a small amount of sulfuric acid gives a liquid product with b.p. 49.5-50° at 7 mm. The elementary analysis, the saponification value and the molecular refraction correspond to the diacetate of the hydrate form of acetone $(CH_3)_2C(OCOCH_3)_2$ which has not previously been described in the literature. The enol acetate of acetone, reported in the literature to have b.p. 90-96.5° [8] was not detected in the reaction products.

Reaction of methylpropyl ketone with acetic anhydride led to a product with a pleasant ethereal odor, b.p. 22.5-23.5° at 4 mm. Its elementary analysis, saponification value and molecular refraction

* It must be pointed out that the enol acetate of cyclopentanone can be prepared and isolated if the reaction is carried out in other conditions. Thus, Mannich and Hancu [3] obtained it, although in very small yield, by heating cyclopentanone with acetic anhydride at 180°.

** For the literature on this problem see the paper of Mousseron and Winternitz [4].

*** Acetone enol acetate has been prepared by another route [8].

correspond to the acetate of the enol form of methylpropyl ketone. One of the two following formulas is possible for the prepared compound:

$CH_2=C(OCOCH_3)-CH-CH_2CH_3$; $CH_3=C(OCOCH_3)-CH_2CH_2CH_3$.

(II) (III)

Formula (II) is more probable: this represents the enol acetate formed as a result of enolization of the methyl group. Thus, Hancu [7] obtained the enol acetates of diethyl- and dipropyl ketones by heating the corresponding ketones with acetic anhydride in presence of sodium acetate; in the case of acetone, however, the enol acetate was not obtained, but mesityl oxide. Bedukian [9] obtained the enol acetates of ketones by heating ketones with acetic anhydride in presence of p-toluenesulfonic acid; he established that in his experimental conditions enolization proceeded at the expense of the methylene and not of the methyl group. We failed to detect the diacetate of the hydrate form of methylpropyl ketone in the products of this reaction.

Consequently, ketones of the aliphatic series in the investigated conditions enter into reaction with acetic anhydride with formation of the diacetates of their hydrate form (acetone) or of the enol acetates (methylpropyl ketone).

In the conditions of this reaction an investigation was also made of the behavior of an aliphatic-aromatic ketone (acetophenone) and of a purely aromatic ketone (benzophenone). We established that acetophenone does not enter into reaction with acetic anhydride; it was almost completely recovered unchanged from the reaction mixture together with an insignificant amount of high-boiling fractions which were probably autocondensation products of acetophenone. Benzophenone likewise does not react with acetic anhydride, not even when heated to a temperature of 100°.

EXPERIMENTAL

1. Reaction of Cyclopentanone with Acetic Anhydride

To a mixture of 28 g freshly distilled cyclopentanone (b.p. 128-130°) and 102 g acetic anhydride (also freshly distilled – b.p. 137-140°) was added 0.26 ml concentrated sulfuric acid; slight heat was developed. The mixture was left for 5 days at room temperature. The red-colored mass was then treated with ice water for decomposition of the unreacted acetic anhydride and then extracted with ether. The aqueous layer was neutralized with sodium carbonate and again extracted with ether. The combined ether extracts were washed with sodium carbonate solution until neutral, then with water, and dried with sodium sulfate. The ether was distilled off and the residue distilled in vacuum (4 mm).

By distillation however, we failed to isolate any constant boiling fraction whatever; the product boiled with constantly increasing temperature from 23 to 75°. A 72-74° fraction, obtained in small amount, crystallized on standing; after two recrystallizations from moderately heated dilute alcohol, the crystals had m.p. 37-39°.

7.49 mg substance: 16.00 mg CO_2; 5.22 mg H_2O. 5.09 mg substance: 10.91 mg CO_2, 3.58 mg H_2O. Found %: C 58.30, 58.49; H 7.80, 7.87. $C_9H_{14}O_4$. Calculated %: C 58.05; H 7.58. Saponification value 608; calculated 603.

A second distillation of the reaction products likewise did not lead to isolation of the enol acetate; a series of new fractions with lower boiling points was obtained; they decolorized bromine water, had a strongly acid reaction and a high saponification value. Thus, the fraction with b.p. 25-30° at 4 mm had saponification value 246 (calculated for the enol acetate of cyclopentanone 445).

When the reaction was conducted over a longer period of time (21 days or 30 days), we again failed to isolate the enol acetate in the pure form; however, when the fractions boiling at 23-26° at 4 mm had been purified with bisulfite solution, they gave closer analytical results (for example, saponification value 402). Potassium permanganate oxidation of a bisulfite-purified fraction gave glutaric acid. The diacetate of the hydrate form of cyclopentanone was obtained in small amounts in all the experiments.

2. Reaction of Acetone with Acetic Anhydride

To a mixture of 23 g acetone, purified through the bisulfite compound (b.p. 55-56°), and 123 g acetic anhydride (b.p. 137-140°) was added 0.42 ml concentrated sulfuric acid. Slight heat was developed. The mixture was left for 13 days at room temperature and acquired a reddish-brown color. The reaction mass was

worked up as in the experiment with cyclopentanone. The residue from the ether distillation was subjected to vacuum distillation, the main bulk coming over at 42-43° at 4 mm and a second distillation giving a small fraction with b.p. 49.5-50° at 7 mm. The product did not decolorize bromine water and was acid to litmus.

4.30 mg substance: 8.22 mg CO_2; 2.94 mg H_2O. 3.59 mg substance: 6.89 mg CO_2; 2.47 mg H_2O. Found %: C 52.17, 52.37; H 7.65, 7.70. $C_5H_8O_4$. Calculated %: C 52.49; H 7.55. Saponification value 676; calculated 700.

8. Reaction of Methylpropyl Ketone with Acetic Anhydride

To a mixture of 28.7 g methylpropyl ketone, purified through the bisulfite compound (b.p. 100-102°), and 102 g acetic anhydride (b.p. 138-140°) was added 0.26 ml concentrated sulfuric acid drop by drop. The mixture was left for 13 days, at the end of which period it had acquired a reddish-brown color. The reaction mixture was worked up in the usual manner. In view of the fact that a sample of the residue after removal of the ether gave a small precipitate when shaken with bisulfite, the whole mass was treated with bisulfite to eliminate the ketone that had not reacted (a total of 2.5 g bisulfite compound was separated). After removal of the ketone, the mixture was worked up in the usual manner. The residue after ether removal was subjected to vacuum distillation, the main bulk (9.5 g) coming over at 24-26° (6 mm); it decolorized bromine water, did not form a precipitate with bisulfite and was neutral to litmus. A second vacuum distillation gave a product with b.p. 22.5-23.5° (4 mm) with an ethereal odor. n_D^{16} 1.4178; d^{20} 0.9043; MR_D 35.70; calculated 35.71.

4.60 mg substance: 11.03 mg CO_2; 3.82 mg H_2O. 6.19 mg substance: 14.87 mg CO_2; 5.09 mg H_2O. Found %: C 65.44, 65.56; H 9.29, 9.20. $C_8H_{12}O_4$. Calculated %: C 65.60; H 9.44. Saponification value 421; calculated 438.

It should be pointed out that the methylpropyl ketone enol acetate that we obtained differs from the enol acetates of other ketones previously prepared by us in that it boils in a narrow temperature interval and has a neutral reaction; the enol acetates of cyclohexanone and its homologs always had an acid reaction and distilled over a fairly wide temperature range.

The residue from the distillation of methylpropyl ketone enol acetate (a very small amount of resinous substances) did not have an odor of acetic anhydride, as had been the case in other reactions in which the diacetates of the hydrate forms had been formed (cyclohexanone and its homologs).

SUMMARY

1. It was established that the reaction of acetic anhydride with cyclopentanone at room temperature in presence of a small amount of concentrated sulfuric acid gave, among other products, the diacetate of the hydrate form of cyclopentanone, not previously described in the literature.

2. In similar conditions acetone forms the diacetate of the hydrate form of acetone, not previously described in the literature. Methylpropyl ketone reacts in the same conditions with formation of the enol acetate.

3. Acetophenone and benzophenone do not enter into reaction with acetic anhydride in these conditions.

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SYNTHESIS OF α-HALO KETONES OF THE ACETYLENE SERIES

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Ketones of the acetylenic series containing a triple bond conjugated with the carbonyl group were first prepared by Nef [1] and later investigated by Moureau [2,3], Andre [4] and others. More recently a method has been developed for the synthesis of the simplest representatives of this series (ethinyl ketones) and some of their chemical transformations have been studied [5]. Compounds of this type, possessing the conjugated system $-C\equiv C-\underset{|}{C}=O$, are distinguished by high reactivity and serve as starting materials for a number of syntheses. Up to now ketones of the acetylenic series containing other functional groups have been unknown. And it is evident that the presence of such groups considerably broadens the range of transformations of these compounds and provides great opportunities for their utilization for synthetic purposes.

This investigation is concerned with the synthesis of ketones of the acetylenic series containing a halogen atom in the α-position to the carbonyl group. It was thought that the synthesis of these compounds could be realized by reacting the sodium derivative of the acetylenic hydrocarbon with the acid chloride of the α-halo acid in accordance with the scheme:

$$RC\equiv CNa + XCOCHXR' \longrightarrow RC\equiv CCOCHXR'.$$

It could be assumed that only the halogen of the acid chloride grouping would enter into the reaction. Such a reaction course is consistent with the reports in the literature about the behavior of metallic derivatives of acetylenic hydrocarbons which readily react with acid chlorides [1,2,3,4] and are alkylated with great difficulty by the action of alkyl halides in a medium of nonpolar solvents [6].

We investigated the preparation of α-halo ketones of the acetylenic series with reference to the reaction of the sodium derivative of phenylacetylene with chloroacetyl chloride. From the reaction mixture was isolated a crystalline substance with the composition $C_{10}H_7OCl$, m.p. 37°, containing halogen, giving a reaction for a multiple bond and a carbonyl group. The structure of this compound was established by reduction with zinc dust in alcohol with addition of acetic acid. Reduction with excess of zinc dust gave benzylacetone (identified in the form of its semicarbazone) and a crystalline substance with m.p. 160-161°, which proved to be identical with the 4,5-diphenyloctanediol-2,7 prepared by Harries and Eschenbach [7] by reduction of benzalacetone with aluminum amalgam. Reduction with a molar equivalent of zinc dust gave a 52% yield of phenylethinylmethyl ketone, which was identified by its dinitrophenylhydrazone and by conversion into phenylmethylpyrazolone. In this case, therefore, the triple bond remains intact on reduction, so that we have direct evidence of the structure of the prepared compound. Consequently the condensation of sodium phenylacetylide with chloroacetyl chloride proceeds according to the above scheme and leads to 1-phenyl-4-chlorobutyne-1-one-3, whose reduction may be represented by the following equation:

$$C_6H_5C\equiv CCOCH_2Cl \longrightarrow C_6H_5C\equiv CCOCH_3$$

$$C_6H_5CHCH_2COCH_3 \leftarrow C_6H_5CH=CHCOCH_3 \longrightarrow C_6H_5CH_2CH_2COCH_3$$

$$C_6H_5CHCH_2COCH_3$$

Other acid chlorides of α-halo acids react with sodium phenylacetylide in a similar manner to chloroacetyl chloride. We performed this reaction with the acid bromides of α-bromopropionic, α-bromobutyric and α-bromoisobutyric acids, and we obtained, respectively, 1-phenyl-4-bromopentyne-1-one-3, 1-phenyl-4-bromohexyne-1-one-3 and 1-phenyl-4-bromomethylpentyne-1-one-3.

The reaction is carried out by adding an ethereal suspension of sodium phenylacetylide to the acid chloride; it proceeds rather violently and is complete after a few hours. In all cases a portion of the phenylacetylene is recovered unchanged even when using a considerable excess of acid chloride. The yields

of acetylenic ketones are about 40% on the average and fall slightly with increasing size of alkyl radical. Data for the compounds prepared appear in the table.

Halo ketones of the acetylenic series

Name	Yield (%)	B.p. (7 mm)	d_4^{25}	n_D^{25}	MR_D Found	MR_D Calc.	EMR_D	M.p. of the 2,4-dinitrophenylhydrazone
1-Phenyl-4-chlorobutyne-1-one-3 (m.p. 37°)	42.5	135-137°	—	—	—	—	—	170-171°
1-Phenyl-4-bromopentyne-1-one-3	47	145-146	1.3668	1.6008	59.36	55.48	3.88	188.5-189
1-Phenyl-4-bromohexyne-1-one-3	37	167.5-168.5	1.3155	1.5880	64.16	60.09	4.07	163-164
1-Phenyl-4-bromo-4-methylpentyne-1-one-3	36	146-148	1.3037	1.5843	64.43	60.09	4.34	173.5-174

As we see from the table, the prepared α-halo ketones are distinguished by a fairly high exaltation of molecular refraction. It is interesting to note that the magnitude of this exaltation is approximately greater by 0.6-0.7 than the exaltation of the corresponding acetylenic ketones not containing a halogen atom [4]. This difference corresponds exactly to the magnitude of the exaltation characteristic of the simplest α-halo ketones (chloroacetone, bromoacetone). Consequently, in our case the exaltation of molecular refraction is composed of the exaltation characteristic of the system $-C\equiv C-\overset{|}{C}=O$, and the exaltation of the system $-COCH_2X$.

All the prepared compounds manifest unsaturation: they decolorize permanganate and bromine water. They readily form derivatives at the carbonyl group; the 2,4-dinitrophenylhydrazones were selected for purposes of characterization since, as far as we are aware, they have the least tendency to form cyclic derivatives due to secondary transformations.

The prepared acetylenic α-halo ketones are characterized by sensitivity to alkaline agents. Alcoholic and aqueous solutions of caustic alkalies in the cold and sodium carbonate solution at higher temperatures bring about almost complete resinification of the halo ketone. The same change occurs when the halo ketone is boiled with an aqueous suspension of barium carbonate. This behavior is undoubtedly associated with the lability of the halogen which, as we know from the work of A. E. Favorsky, S. N. Danilov and others, is characteristic of α-halo ketones in general; in our case the lability of the whole system increases markedly due to the presence of the neighboring double bond.

By contrast, the prepared compounds are fairly stable toward acid agents. Heating of a methyl alcoholic solution of phenylethinylchloromethyl ketone with sodium sulfate solution in a sulfuric acid medium results in development of a characteristic reddish-brown color with an intense green fluorescence. This phenomenon is possibly associated with formation in the reaction mixture of a compound of the oxonium type due to cyclization of the formed chlorine-containing α-diketone. The cause of this phenomenon has not yet been closely studied.

EXPERIMENTAL

1. 1-Phenyl-4-chlorobutyne-1-one-3

To a solution of 30.6 g (0.3 mole) phenylacetylene and 100 ml absolute ether is added, with cooling, 7.9 g (0.3 mole) finely sliced sodium. At the conclusion of the energetic reaction, the mixture is refluxed for an hour until the metal has completely dissolved. The resultant suspension of sodium phenylacetylide is stirred, with cooling (ice-salt) in small portions into a solution of 35 g chloroacetyl chloride in 50 ml absolute ether in the course of an hour. After all has been added, the bath temperature is raised gradually to room temperature and the stirring continued for 4 hours. Addition is then made to the mixture of 150 ml cooled 5% hydrochloric acid, and the mixture is stirred for another 30 minutes. The ether layer is separated and the aqueous layer is extracted with ether; the combined extracts are washed with cold 1% sodium carbonate solution and dried over calcium chloride. The ester is distilled off and the residue fractionated in vacuum. The following fractions (at 7 mm) were collected: 1) to 40° 9.0 g; 2) 40-136° 1.5 g; 3) 136-138° 15.0 g; 4) residue 10.0 g.

The first fraction was unreacted phenylacetylene; it may be reused for synthesis. The third fraction rapidly crystallized almost completely. After recrystallization from ligroine it formed colorless needles with m.p. 37°. Yield 14.5 g.

Found %: C 66.85, 66.78; H 3.82, 3.78. $C_{10}H_7OCl$. Calculated %: C 67.22; H 3.90.

The substance is readily soluble in organic solvents, less soluble in ligroine, insoluble in water. It rapidly decolorizes a solution of permanganate in acetone and a solution of bromine in chloroform.

Dinitrophenylhydrazone. Prepared by the usual method in glacial acetic acid, from which it also recrystallizes in fine, golden needles with m.p. 170-171°.

Found %: N 15.82, 15.72. $C_{16}H_{11}O_4N_4Cl$. Calculated %: N 15.62.

Insoluble in water, benzene, ether; poorly soluble in alcohol; soluble in acetic acid.

II. 1-Phenyl-4-bromopentyne-1-one-3

This compound is prepared by a similar method from sodium phenylacetylide (from 15.32 g phenylacetylene, 3.9 g sodium in 70 ml absolute ether) and a solution of 36.6 g (0.17 mole) α-bromopropionyl bromide in 40 ml absolute ether. The following fractions were collected on distillation in vacuum: 1) to 40° 5 g (unreacted phenylacetylene); 2) 40-147° 1.5 g; 3) 147-152° 14.0 g; 4) residue 3.5 g.

A second distillation of the third fraction gave 11 g 1-phenyl-4-bromopentyne-1-one-3 with b.p. 145-146° at 6 mm. Amber-colored oil, slowly darkening when kept.

Found %: C 55.67, 55.59; H 3.79, 3.74. $C_{11}H_9OBr$. Calculated %: C 55.69; H 3.79.

The dinitrophenylhydrazone consists of fine yellow needles with m.p. 188.5-189°. Poorly soluble in alcohol, insoluble in water, soluble in acetic acid. Found %: N 13.29, 13.46. $C_{17}H_{13}O_4N_4Br$. Calculated %: N 13.45.

III. 1-Phenyl-4-bromohexyne-1-one-3

Prepared from 15.3 g (0.15 mole) phenylacetylene, 3.7 g sodium and 39.0 g (0.17 mole) α-bromobutyryl bromide. After vacuum-distillation of the reaction product, the following fractions were collected (at 8 mm): 1) to 40° 4.5 g (unreacted phenylacetylene); 2) 40-165° 1.5 g; 3) 165-177° 9.9 g; 4) residue 6.3 g.

A second distillation of the third fraction gave 9.7 g 1-phenyl-4-bromohexyne-1-one-3 with b.p. 167.5-168.5° at 7 mm. Amber-colored oil, slowly darkening when kept.

Found %: C 57.24, 57.33; H 4.45, 4.48. $C_{12}H_{11}OBr$. Calculated %: C 57.39; H 4.38.

Dinitrophenylhydrazone. Orange yellow needles with m.p. 163-164°. Insoluble in water, poorly soluble in alcohol, soluble in acetic acid.

Found %: N 12.94, 12.79. $C_{18}H_{15}O_4N_4Br$. Calculated %: N 12.99.

IV. 1-Phenyl-4-bromo-4-methylpentyne-1-one-3

Prepared from 15.3 g (0.15 mole) phenylacetylene, 3.7 g sodium and 39.0 g (0.17 mole) α-bromoisobutyryl bromide. The following fractions were collected after vacuum-distillation (7 mm) of the reaction product: 1) to 40° 5.0 g (unreacted phenylacetylene); 2) 40-145° 4.0 g; 3) 145-150° 13.0 g; 4) residue 5.2 g.

A second distillation of the third fraction gave 8.8 g 1-phenyl-4-bromo-4-methylpentyne-1-one-3 with b.p. 146-148° at 7 mm. Amber oil, slowly darkening when kept.

Found %: C 57.28, 57.09; H 4.44, 4.28. $C_{12}H_{11}OBr$. Calculated %: C 57.39; H 4.38.

Dinitrophenylhydrazone. Orange-yellow needles with m.p. 173.5-174°. Insoluble in water, poorly soluble in alcohol, soluble in acetic acid.

Found %: N 13.08, 13.11. $C_{18}H_{15}O_4N_4Br$. Calculated %: N 12.99.

V. Reduction of 1-Phenyl-4-chlorobutyne-1-one-3 with Excess of Zinc Dust

To a solution of 7.5 g chloroketone in 150 ml alcohol was added 50 ml acetic acid followed, in small portions, by 13.5 g zinc dust, the temperature of the mixture being kept at about 40°. The reaction was completed by refluxing the mixture at 50°. The hot solution was then filtered from the excess of zinc dust,

and the alcohol was distilled off. The residue formed two layers. It was extracted with ether and the extract washed with water and dried over sodium sulfate. On the following morning the crystals were filtered off from the extract (yield of crystals 0.5 g). After recrystallization from alcohol the product formed colorless needles with m.p. 160.5°. The ether was driven off the extract and the residue therefrom was distilled in vacuum to give the following fractions (at 13 mm): 1) to 110° a few drops; 2) 110-115° 2.0 g; 3) 115-150° a few drops; 4) 150-200° 1.5 g.

The fourth fraction crystallized completely in the receiver. The crystals were pressed and recrystallized from alcohol-ether mixture to give 0.9 g colorless crystals with m.p. 160° which did not depress the m.p. in admixture with the substance crystallizing from the extract. The mixed sample of both portions of the substance with 4,5-diphenyloctadione-2,7 [7] does not give a melting point depression.

The second fraction was converted by the usual method into the semicabazone which formed colorless crystals (from aqueous methyl alcohol) with m.p. 141-142°. A mixed sample with the semicarbazone of benzylacetone did not give a melting point depression.

VI. Reduction of 1-Phenyl-4-chlorobutyne-1-one-3 with a Molar Amount of Zinc Dust

Into a solution of 5.0 g chloroketone in 175 ml 7% methyl alcohol is introduced, portionwise(0.2 g portions over a period of an hour,)2 3 g zinc dust, and addition is made simultaneously, in 2 ml portions, of 20 ml 25% acetic acid. Each portion of zinc dust was only introduced after the previous one had completely dissolved. The mixture was then shaken for another hour and then filtered, and the methyl alcohol driven off. The residue formed layers and was extracted with ether. The extracts were twice washed with water and dried over sodium sulfate. The ether was driven off and the residue distilled in vacuum, the following fractions being collected (at 5 mm): 1) to 110° a few drops; 2) 110-112° 2.1 g (52% of the theoretical); 3) 112-120° 0.4 g.

The second fraction had the following constants after a second vacuum distillation: b.p. 110-111° at 5 mm; n_D^{18} 1.5742; d_4^{18} 1.0257. (Literature data for phenylethinylmethyl ketone [4]. b.p. 122-124° at 13 mm; n_D^{18} 1.5728, d_4^{18} 1.024).

The dinitrophenylhydrazone formed orange-yellow crystals with m.p. 185-186°. A mixed test with the dinitrophenylhydrazone of phenylethinylmethyl ketone did not give a melting point depression.

Phenylmethylpyrazolone. Prepared by the method of Moureau and Brachin [8] and had m.p. 123-124° after recrystallization from 25%alcohol. A mixed test with an authentic specimen of phenylmethylpyrazolone did not give a melting point depression.

SUMMARY

1. Reaction of sodium phenylacetylide with acid chlorides of α-halo-substituted acids gives α-halo ketones of the acetylene series. Preparation was accomplished by this method for the first time of: 1-phenyl-4-chlorobutyne-1-one-3; 1-phenyl-4-bromopentyne-1-one-3; 1-phenyl-4-bromohexyne-1-one-3; and 1-phenyl-4-bromo-4-methylpentyne-1-one-3.

2. The structure of the prepared compounds was proved by reduction of the first member of the series, 1-phenyl-4-chlorobutyne-1-one-3, with zinc dust to phenylethinylmethyl ketone. When using excess of reducing agent the reaction leads to benzylacetone and 4,5-diphenyloctadione-2,7.

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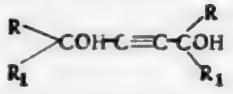
METHODS OF DETERMINATION OF THE STRUCTURE OF TERTIARY ACETYLENIC ALCOHOLS AND OF γ-ACETYLENIC GLYCOLS

II. DETERMINATION OF THE STRUCTURE OF ACETYLENIC ALCOHOLS, γ-GLYCOLS AND DIACETYLENIC GLYCOLS BY OZONIZATION AND BY THE SPECTROGRAPHIC METHOD

A. I. Lebedeva, T. A. Mishnina and R. P. Ryskina

We know from previous investigations [1] that oxidation of acetylenic glycols with potassium permagnate in aqueous or acetone solution gives a ketone, an α-hydroxy acid and oxalic acid, i.e. the same products that must also be formed on oxidation of diacetylenic glycols with a conjugated system of triple bonds. Consequently this method cannot be used for determination of the structure of glycols having the general formula



and

We decided to apply ozonization and ultraviolet spectrographic analysis for the determination of the structure of these compounds.

Although the ozonization of acetylenic compounds was first given attention over 45 years ago, this field has still not been exhaustively investigated. There are still no unambiguous answers to the question of the structure of the ozonides of the acetylenic series, of the mechanism of the processes taking place during ozonization and during decomposition of the ozonides. Some investigators believe [2] that ozonization of the acetylenic bond proceeds through the stage of formation of 1,2-diketones which are then oxidized by hydrogen peroxide formed by decomposition of the ozonides, giving the saturated acids. Such diketones were isolated in the ozonization of diphenylacetylene and benzylphenylacetylene [3]. With the help of ultraviolet spectrography, Kahn and Newman [4] succeeded in showing that ozonization of stearolic acid gives 9,10-diketostearic acid.

We were unable to find in the literature any references to the ozonization of acetylenic γ-glycols and diacetylenic glycols. Before undertaking actual ozonizations, therefore, we found it necessary to select uniform conditions with respect to solvent, temperature, method of decomposition and analysis of the products of ozonolysis. In preliminary experiments it was established that the acetylenic compounds under investigation absorbed, at the most, 60-65% of the amount of ozone introduced. It was also established that methyl alcohol and ethylacetate react with ozone during ozonization in our conditions; we therefore chose chloroform as solvent. Ozonization was performed at −20° when the ozonization temperature was lowered to −60°, the starting material came out of solution. Determinations were made throughout periods of 15 minutes of the amount of ozone entering the reaction vessel and leaving it. Ozonization was stopped after addition of the theoretically calculated amount of ozone. In Figure 1 (see also Table 3) on the ordinates is plotted the amount of ozone absorbed in unit time, the abscissas show the period of time. We see from the curves that the rate of ozonization of tetraethylbutynediol was constant up to the absorption of one molecule of ozone, and then fell rather sharply. In the ozonization of the diacetylenic compound 3,8-dimethyl-4,6-decadiyne 3,8-diol, the rate was constant up to absorption of approximately one molecule of ozone, after which it gradually dropped until two molecules of ozone had been taken up. In this respect the rate of ozonization of the $-C\equiv C-C\equiv C-$ bonds is reminiscent of the rate of ozonization of conjugated dienic systems. Harries [5] had already established that in compounds containing two conjugated double bonds, the first molecule of ozone adds on much more rapidly than the second. We also know from a later investigation [6] that in the ozonization of compounds with two or three conjugated double bonds, only one molecule of ozone adds on quickly, and a gradual fall in the rate of ozone absorption is then observed.

During the ozonization of diethyldecadiynediol we observed that the solution changed color. In the first period the color became yellow; in the second period it changed from light-green to blue.

In the ozonization of tetra-p-tolylbutynediol and methyl-p-tolylethinyl carbinol, the speed is low and gradually decreases throughout the entire process. No inflection whatever could be observed in the curve after addition of one molecule of ozone. If we stopped the ozonization after addition of one molecule of ozone, we recovered up to 60% of

the starting material unchanged. All this supported the view that in the case of aromatic constituents, ozone reacts not only with the triple bond but also with the aromatic nucleus. Results of analyses of the ozonolysis products appear in Table 2.

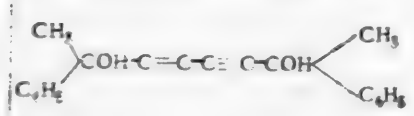
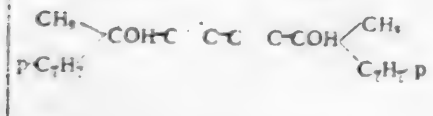
We see from this table that the structure of acetylenic γ-glycols of the aliphatic series can be determined by quantitative ozonization with arbitrary quantitative allowance for the ozonolysis products. This method, however, has a number of limitations. With increasing molecular weight of the substituents, the yield of oxalic acid increases while that of α-hydroxy acids decreases. The increase in oxalic acid yield is particularly large in ozonization of aliphatic-aromatic acetylenic glycols. Another drawback is the rather long period involved in the process of ozonization and in analysis of the ozonolysis products.

In the light of the above facts we decided to apply the spectrographic method to analysis of the diacetylenic compounds. We know that acetylenic compounds in which the triple bond is not conjugated with another unsaturated bond or with a carbonyl, nitro or nitroso group possess a strong absorption in the ultraviolet in the short wave region not higher than 2200 A.

When the triple bond is conjugated, however, with one or several double or triple bonds, a considerable shift occurs in the maximum of light absorption toward the longer wave region and a significant increase in the intensity of absorption. Using the method of variable thickness of layer, we plotted on the SP-22 spectrograph the absorptions of the following compounds: 1) 3,8-dimethyl-4,6-decadiyne-3,8-diol; 2) 3,8-diethyl-4,6-decadiyne-3,8-diol; 3) 4,9-dimethyl-5,7-dodecadiyne-4,9-diol; 4) 2,9-dimethyl-3,8-diisopropyl-4,6-decadiyne-3,8-diol, and 5) 2,7-di-p-tolyl-3,5-octadiyne-2,7-diol. The plots showed that all of the investigated diacetylenic glycols have an absorption maximum in the 2400-2500 Å region. For quantitative characterization of the intensity of absorption, plots were constructed, with the SF-11 spectrophotometer (Beckmann system), of the absorption curves of the following compounds: 1) 2,5-di-p-tolyl-3-hexyne-2,5-diol; 2) 3,8-diethyl-4,6-decadiyne-3,8-diol; and 3) 2,7-di-p-tolyl-3,5-octadiyne-2,7-diol.

For comparison with our own results, Table 1 also contains data of other investigators. Some of these data were published when we had already completed the experimental part of the present investigation.

TABLE 1

No.	Formula	λ maximum (in A)	K	Literature
		2290	310	[7]
		2410	300	
1	$(CH_3)_2COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(CH_3)_2$	2560	180	
2	$(C_2H_5)COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(C_2H_5)_2$	2410	317	Our data
		2560	201	
3		2445	1020	[8]
		2580	900	
4	$(C_6H_5)_2COH{-}C{\equiv}C{-}C{\equiv}C{-}COH(C_6H_5)_2$	2485	2240	[8]
		2610	1660	
5		2440	1550	
		2580	1170	Our data
		2620 •	1170	
		2720	660	
6		2620	388	Our data
		2720	328	

• The principal maximum of toluene is at 2620 Å.

It is seen from the data of Table 1 that diacetylenic glycols of the aliphatic series possess not less than two characteristic absorption maxima in the ultraviolet at 2410 and 2560 A.

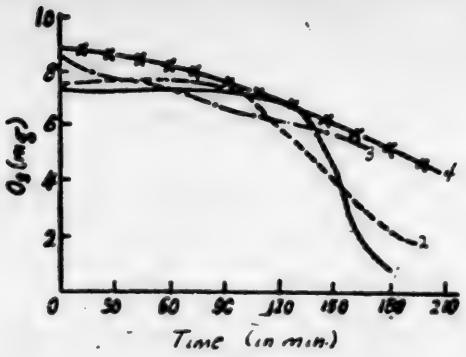


Fig. 1.

1) Tetraethylbutynediol; 2) dimethyldecadiynediol; 3) tetra-p-tolylbutynediol; 4) methyl-p-tolylethinyl carbinol.

Consequently the ultraviolet method permits the possibility of establishing the presence in the investigated product of a compound with a conjugated system of triple bonds.

EXPERIMENTAL

Preparation of 4,9-dimethyl-5,7-dodecadiyne-4,9-diol. 20 g methyl-n-propylethinyl carbinol was added to a mixture consisting of 60 g ammonium chloride, 20 g cuprous chloride and 250 ml water. Oxygen was passed through the mixture with good stirring for 2 hours. The resultant precipitate was filtered off and the solution was extracted with ether. A total of 18.6 g solid product was obtained; this was repeatedly recrystallized from a mixture of benzene and ligroine (40-60°) and then from petroleum ether to form crystals in the form of small needles with m.p. 74-75°.

0.1038 g substance: 0.2877 g CO_2; 0.0937 g H_2O.
0.1886 g substance: 17.95 g benzene: Δt 0.230°.
0.0657 g substance: 15.4 ml CH_4 (14°, 773 mm).
Found %. C 75.61; H 10.10. M 222, act. H-atoms 2.18. $C_{14}H_{18}(OH)_2$. Calculated %: C 75.65; H 9.98. M 234, act. H-atoms 2.00.

From the residue after recrystallization could be separated crystals, melting at 100-104° (gradually), in very small quantity, these gave a melting point depression with the first isomer.

Preparation of 2,9-dimethyl-3,8-diisopropyl-4,6-decadiyne-3,8-diol. From 18 g diisopropylethinyl carbinol (technical), by the preceding method, was prepared 6.4 g of a solid product which after recrystallization from dilute alcohol came down in the form of lustrous scales with m.p. 118-119°.

The literature gives m.p. 115° [9].

The presence in the molecule of a diacetylenic glycol of aromatic substituents possessing their own specific absorption maxima has no appreciable influence on the position of the maxima characteristic of the $-C\equiv C-C\equiv C-$ bonds. This is demonstrable with particular clarity by the curves obtained when investigating acetylenic and diacetylenic compounds in the ultraviolet in the SF-11 spectrograph (Figs. 2 and 3).

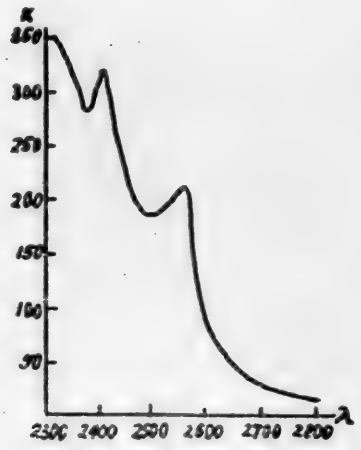


Fig. 2. Dimethyldecadiynediol.

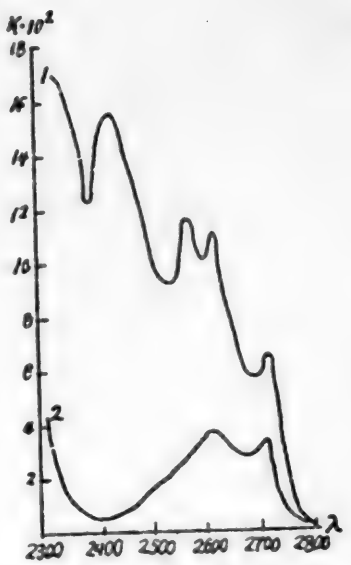


Fig. 3.
1) Di-p-tolyloctadiynediol; 2) symm-dimethyldi-p-tolylbutynediol.

TABLE 2

Preparation No.	Name of compound and formula	Physical constants	Quantity	
			Of compounds taken (in g)	Of ozone absorbed (in g)
				exper. / theor.
1	Tetramethylbutynediol $(CH_3)_2COH-C\equiv C-COH(CH_3)_2$	M.p. 94-95°	4.0	3.36 / 1.35
2	Tetraethylbutynediol $(C_2H_5)_2COH-C\equiv C-COH(C_2H_5)_2$	M.p. 80-81°	4.0	1.02 / 0.97
3	Dimethyldiethylbutynediol $C_2H_5(CH_3)COH-C\equiv C-COH(CH_3)C_2H_5$	M.p. 52-53°	4.0	0.88 / 1.13
4	Diethylethinyl carbinol $(C_2H_5)_2COH-C\equiv CH$	B.p. 136-138°	4.9	2.00 / 1.71
5	Methyl-p-tolylethinyl carbinol $p\text{-}C_7H_7(CH_3)COH-C\equiv CH$	M.p. 34-35°	4.0	1.28 / 1.20
6	Tetra-p-tolylbutynediol $(p\text{-}C_7H_7)_2COH-C\equiv C-COH(C_7H_7\text{-}p)_2$	M.p. 154-155°	4.0	0.46 / 0.43
6a	Dimo	M.p. 154-155°	4.0	3.51 / 0.43
7	3,8-Dimethyl-4,6-decadiyne-3,8-diol $C_2H_5(CH_3)COH-C\equiv C-C\equiv C-COH(CH_3)C_2H_5$	M.p. 89-90°	2.0	0.98 / 0.98
8	4,9-Dimethyl-5,7-dodecadiyne-4,9-diol $n\text{-}C_3H_7(CH_3)COH-C\equiv C-C\equiv C-COH(CH_3)C_3H_7\text{-}n$	M.p. 74-75°	2.0	0.83 / 0.87

The remaining diacetylenic glycols were synthesized in the same manner.

Ozonization*. A weighed amount of the compound to be ozonized was dissolved in 40 ml chloroform and placed in a reaction vessel externally cooled with a mixture of ice and salt. An exception was represented by tetramethylbutynediol which we ozonized in solution in ethyl acetate because it was insoluble in chloroform. Through the reaction vessel was passed dry ozonized oxygen containing 4-6% ozone. The amount of ozone entering and leaving the reaction vessel during each 15 minute period was determined by titration with thiosulfate, while the amount of ozone absorbed was determined by difference. In the majority of experiments ozonization was concluded after the theoretical amount of ozone had been absorbed although in many experiments the absorption of ozone continued with nearly the same velocity, as can be seen from the results enumerated in Table 3. The rate of ozonization is expressed in Table 3 in ml thiosulfate ($T_{Na_2S_2O_3}$ = = 0.00221 g/ml).

The prepared ozonides were worked up in the following manner: the solvent was filtered at the pump at room temperature the ozonide was decomposed with water with heating until the oily drops had disappeared, and potassium carbonate was added to the solution until the reaction was alkaline. The volatile neutral products were distilled into an acetic acid solution of p-nitrophenylhydrazine, and the nonvolatiles were extracted with ether. For the purpose of extraction of the hydroxy acids, the acidified (with sulfuric acid) solution was extracted with ether in a separating funnel; for extraction of the oxalic acid, the solution was treated for 50-60 hours in a Soxhlet. The oxalic acid was determined as the calcium salt. The yield of oxalic acid (in %) was calculated in relation to the amount of prepared ozonide. In experiments 1 and 6a (Table 2) much more than the theoretically calculated amount of ozone was passed through. When the theoretical amount of ozone was passed through, much of the starting material was recovered unchanged.

* Ozonization was carried out by the method of A. I. Yakubchik [10].

Table 2

Of ozonide obtained (in g) exper. / theor.	Products of ozonolysis: Neutral (in g)	Hydroxy acids: Yield (in g)	Hydroxy acids: M.p.	Oxalic acid: (g)	Oxalic acid: (%)
5.0 / 5.3	Acetone (traces)	$(CH_3)_2COH-COOH$ (4.1)	79-80°	None	None
4.9 / 5.0	Diethyl ketone (traces)	$(C_2H_5)_2COH-COOH$ (3.6)	77-78	0.002	0.11
5.6 / 5.1	None	$C_2H_5(CH_3)COH-COOH$ (2.3)	65-66	0.011	0.52
4.5 / 7.0	Diethyl ketone (traces)	$(C_2H_5)_2COH-COOH$ (2.4)	77-78	0.055	2.16
4.8 / 5.2	Methyl-p-tolyl ketone (1.77)	$p-CH_3C_6H_4COOH$ (1.8)	173	0.042	2.00
—	Tetra-p-tolylbutynediol (2.50)	$(p-C_7H_7)_2COH-COOH$ (1.3)	131-132	None	None
4.5 / 4.4	Resin	$p-CH_3C_6H_4COOH$ (1.8)	176-177	0.092	11.35
2.7 / 3.0	Methylethyl ketone (0.10)	$C_2H_5(CH_3)COH-COOH$ (1.7)	65-66	0.300	30.0
2.5 / 2.9	Methyl-n-propyl ketone (0.1)	$n-C_3H_7(CH_3)COH-COOH$ (1.8)	50-51	0.250	30.6

TABLE 3

Preparation No	Name of compound	Amount of ozone absorbed each 2 min. (in ml thiosulfate)
1	Tetramethylbutynediol	6.7; 6.6; 6.8; 6.4; 6.0. 6.1. 6.1; 1.2; 0.8
2	3,8-Dimethyl-4,6-decadiyne-3,8-diol	7.0; 6.9; 6.9; 6.9; 6.4; 6.0; 5.5; 4.4; 3.0; 2.4; 1.8.
3	Tetra-p-tolylbutynediol	10.6; 7.3; 7.1; 6.7; 6.6.
4	Methyl-p-tolylethinyl carbinol	8.0; 7.9; 7.7; 7.6; 7.1; 6.9; 6.4; 6.3; 6.2; 5.6; 5.1; 5.0; 4.5.

In experiment 1, the ozone apparently reacted with the solvent, while in experiments 6 and 6a it reacted with the aromatic nucleus of the substituents entering into the composition of the acetylenic compounds. In experiment 6 the ozonide was decomposed without distillation of the solvent because the ozonide was otherwise obtained in the form of a polymer which was not decomposed either by water or by an aqueous solution of potassium iodide.

After distillation of the ether, the hydroxy acids were recrystallized from benzene. In experiment 6a, p-toluic acid separated instead of di-p-tolylglycolic acid.

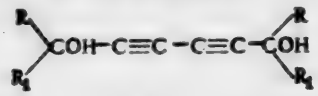
Spectroscopic analysis of the compounds was carried out in ethyl alcohol solution: an 0.5% solution was taken with the SP-22 spectrograph, a solution of 0.03-0.01 moles per liter was taken with the SF-11.

SUMMARY

1. The structure of acetylenic γ-glycols of the aliphatic series can be determined by quantitative ozonization followed by quantitative analysis of the products of ozonolysis. The rate of ozonization of these glycols is constant up to absorption of the theoretical amount of ozone, after which it falls fairly sharply.

2. The rate of ozonization of aliphatic-aromatic acetylenic alcohols and γ-glycols falls slowly throughout the whole process of ozonization; no inflection whatever is observed in the curve after addition of one molecule of ozone. A fairly large amount of oxalic acid (2-10%) is found among the products of ozonolysis, so that this method is little suited to the determination of the structure of these compounds.

3. The structure of diacetylenic glycols of the type of



where R and R_1 are aliphatic substituents may be determined by quantitative ozonization. The rate of ozonization of these glycols is constant up to absorption of one molecule of ozone, after which it gradually begins to drop.

4. Diacetylenic glycols with the above structure possess two characteristic maxima in the ultraviolet at 2140 A and 2560 A. The position of the maxima does not change appreciably when R and R_1 are aromatic radicals, but other maxima appear which correspond to the aryl substituents. The ultraviolet method is applicable to the analysis of diacetylenic glycols containing a conjugated system of triple bonds.

5. The diacetylenic glycol 4,9-dimethyl-5,7-dodecadiyne-4,9-diol has been synthesized for the first time, and it has been shown that the maxima of the absorption spectra of this compound in the ultraviolet are in the region of 2400 and 2600 A.

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THE PROBLEM OF THE FORMATION OF ORGANOMETALLIC COMPOUNDS BY REACTION OF AROMATIC SILANES WITH METALLIC CHLORIDES

I. FORMATION OF ORGANOALUMINUM COMPOUNDS BY REACTION OF PHENYLCHLOROSILANES WITH $AlCl_3$

A. Ya. Yakubovich and G. V. Motsarev

The reaction of aromatic silanes with $AlCl_3$ has been studied with reference to compounds such as diphenyldichlorosilane [1], tetraphenylsilane [2] and triethylphenylsilane [3]. In these cases $AlCl_3$ proved to be an extremely active dearylating agent which brought about cleavage of the organosilicon molecules at the Si—C bond. It was established that this cleavage is effected with great ease even in ordinary conditions and is accompanied by formation of aromatic organoaluminum compounds. This was proved by transformation of the latter into benzene by the action of water.

These data actually comprise all that is known about the action of $AlCl_3$ on aromatic organosilicon compounds. There are no data at all for the influence of the ratio of components (silane and $AlCl_3$) or for the effect of substituents in the aromatic nucleus on the course and on the results of reaction between aromatic silanes and $AlCl_3$. Moreover, the formation of benzene by treatment of the products with water constitutes the sole evidence that organoaluminum compounds are formed and cannot be regarded as conclusive evidence.

For these reasons we undertook an investigation of these reactions, starting from phenyltrichlorosilane, diphenyldichlorosilane and their derivatives.

We first studied the unsubstituted phenyltrichlorosilane. It was found that this compound, just like the other silanes, reacts with freshly sublimed $AlCl_3$ with cleavage at the Si—C bond even at a temperature of 30-35°. The product of this reaction, apart from $SiCl_4$ (isolated in a yield of 50% of the theoretical), is actually phenylaluminum dichloride, as could be inferred not only from the formation of benzene by treatment with water (after distilling off the $SiCl_4$) but also from the ease of substitution of the $AlCl_2$ residue by the CH_3CO- or PCl_2- group when reacted with CH_3COCl or PCl_3.

$$C_6H_5SiCl_3 + AlCl_3 \longrightarrow C_6H_5AlCl_2 + SiCl_4; \quad (1)$$

$$C_6H_5AlCl_2 + 3H_2O \longrightarrow C_6H_6 + Al(OH)_3 + 2HCl; \quad (2)$$

$$C_6H_5AlCl_2 + CH_3COCl \longrightarrow C_6H_5COCH_3 + AlCl_3; \quad (3)$$

$$C_6H_5AlCl_2 + PCl_3 \longrightarrow C_6H_5PCl_2 + AlCl_3. \quad (4)$$

Yields of benzene, acetophenone and $C_6H_5PCl_2$ in reactions (2), (3) and (4) were respectively 55.5, 75.0 and 83.4%.

Diphenyldichlorosilane also reacts with $AlCl_3$ at the ordinary temperature, but the reaction course depends on the molar ration of components. Thus with a molar ration of diphenyldichlorosilane to $AlCl_3$ of 1:1 at 30-35°, the reaction products (after decomposition of the reaction mass with water) were benzene (isolated in amount corresponding to a yield of 38% of the theoretical) and a resin (formed by hydrolysis of the phenyltrichlorosilane formed on cleavage) in yield of 65% of the theoretical:

$$(C_6H_5)_2SiCl_2 + AlCl_3 \longrightarrow C_6H_5SiCl_3 + C_6H_5AlCl_2$$

$$C_6H_5SiCl_3 \xrightarrow{+H_2O} (C_6H_5SiO_{1.5})_p$$

$$C_6H_5AlCl_2 \xrightarrow{+3H_2O} C_6H_6 + Al(OH)_3 + 2HCl.$$

With a molar ratio of reactants of 1:2 at 30°, there are formed silicon tetrachloride (yield 60%) and benzene (yield 61.2%), the latter due to decomposition by water of the residue after distilling off the silicon tetrachloride.

$$(C_6H_5)_2SiCl_2 + 2AlCl_3 \longrightarrow SiCl_4 + 2C_6H_5AlCl_2 \quad (6)$$
$$\downarrow +3\,H_2O$$
$$\longrightarrow C_6H_6 + Al(OH)_3 + 2HCl$$

Derivatives of phenylchlorosilanes containing nuclear substituents that were selected for this investigation were p-chloro- and p-bromophenyltrichlorosilanes, as well as (p-chlorophenyl)-phenyldichlorosilane, all prepared with the help of the Grignard synthesis [4].

Halogen-substituted phenylchlorosilanes behave with $AlCl_3$ like unsubstituted phenyl derivatives of silane.

These cleavage reactions undoubtedly lead to formation of organoaluminum compounds containing halogen atoms in the phenyl ring:

$$C_6H_4XSiCl_3 + AlCl_3 \longrightarrow C_6H_4XAlCl_2 + SiCl_4 \quad (7)$$

where X = Cl, Br, etc.

This follows both from the formation of the corresponding halobenzenes by the action of water on the cleavage products and from their reactions with acetyl chloride and phosphorus trichloride which were studied for p-chloro- and p-bromo- phenyltrichlorosilanes:

$$p\text{-}C_6H_4Cl(Br)SiCl_3 + AlCl_3 \longrightarrow p\text{-}C_6H_4Cl(Br)AlCl_2 + SiCl_4; \quad (8)$$

$$p\text{-}C_6H_4Cl(Br)AlCl_2 + CH_3COCl \longrightarrow p\text{-}C_6H_4Cl(Br)COCH_3 + AlCl_3; \quad (9)$$

$$p\text{-}C_6H_4Cl(Br)AlCl_2 + PCl_3 \longrightarrow p\text{-}C_6H_4Cl(Br)PCl_2 + AlCl_3. \quad (10)$$

The yields of $p\text{-}C_6H_4ClCOCH_3$, $p\text{-}C_6H_4ClPCl_2$ and $p\text{-}C_6H_4BrPCl_2$ in reactions (8), (9) and (10) were respectively 53, 77.4 and 72.6%.

(p-Chlorophenyl) phenyldichlorosilane reacts with $AlCl_3$ in a similar manner to diphenyldichlorosilane; in this case we may have either complete or partial cleavage of the molecule, depending on molar ratios of reactants.

On mixing $(p\text{-}C_6H_4Cl)\,C_6H_5SiCl_2$ with $AlCl_3$ in 1:1 molar ratio, cleavage takes place in the first instance of that radical which contains the substituent as indicated by the isolation from the reaction products (after decomposition of the reaction mass with water) of chlorobenzene and resin (the latter formed by hydrolysis of the $C_6H_5SiCl_3$ resulting from the cleavage).

$$\left.\begin{matrix} p\text{-}C_6H_4Cl \\ C_6H_5 \end{matrix}\right\rangle SiCl_2 + AlCl_3 \longrightarrow C_6H_5SiCl_3 + p\text{-}C_6H_4ClAlCl_2 \quad (11)$$
$$\downarrow +H_2O \qquad \downarrow +3H_2O$$
$$(C_6H_5SiO_{1.5})p \longrightarrow C_6H_5Cl + Al(OH)_3 + 2HCl$$

Consequently the introduction of halogen atoms into the aromatic nucleus of a chlorosilane intensifies the reactivity of the Si—C bond toward $AlCl_3$.

It should be noted that the above-described readily proceeding reactions with $AlCl_3$ of phenylchlorosilanes and their derivatives containing a substituent in the aromatic nucleus show that the replacement of SiX$_3$ groups by $AlCl_2$ residues may evidently be utilized as a method of synthesis of organoaluminum compounds of the aromatic series containing various substituents in the nucleus. The field of investigation is an interesting one when we consider that the possibilities of preparation of this type of organosilicon compound are rather wide and that the transformations of the organoaluminum compounds are very diverse and proceed easily.

EXPERIMENTAL

Reaction of Phenyltrichlorosilane with $AlCl_3$

a) Preparation of benzene. To 5.0 g (0.023 mole) phenyltrichlorosilane is added 3.1 g (0.023 mole) freshly

sublimed aluminum chloride. Addition of the latter is accompanied by slight heating of the mixture which acquires a red color. The mixture is left for 48 hours at 25-35°. The liquid mass is carefully distilled in vacuum from the reaction flask on a water bath through a condenser. In the receiver, cooled with acetone-carbon dioxide mixture (−60°), was collected a liquid with b.p. 55-57° and a pungent odor. The b.p. and density (d_4^{20} 1.4840) were identical with those of silicon tetrachloride. Yield 2.0 g or 50% of the theoretical.

The brown, semisolid residue in the reaction flask was carefully (at −50°) decomposed with water and distilled with steam. The layer of liquid on the surface of the aqueous distillate was extracted with ether and dried over calcium chloride. After removing the ether, the residue was distilled on the water bath to give a liquid with b.p. 79-81°, identical in respect to b.p. and density (d_4^{20} 0.879) with benzene. Yield 1.0 g or 55.5% of the theoretical. For further identification the benzene was converted with nitration mixture into a crystalline substance which melted at 89.5° after recrystallization from alcohol and drying. The m.p. is that of m-dinitrobenzene. Yield 81% of the theoretical, calculated on the benzene.

b) Preparation of acetophenone. To 5.0 g (0.023 mole) phenyltrichlorosilane was added 3.1 g (0.023 mole) freshly sublimed aluminum chloride. To the residue remaining after distillation of the silicon tetrachloride (see preceding experiment) was added 2.0 g acetyl chloride in the cold. The mixture was thereupon heated for ½ hour at 50-60°, after which it was carefully treated with iced water while cooling (−30°). The separated oil was extracted with ether and the ethereal solution was washed with water and dried over calcium chloride. The ether was distilled off and the oily residue partly crystallized on standing. The crystals were separated by freezing the oil at 0°. M.p. 20.2° (from alcohol). A mixed test of these crystals with synthetic acetophenone did not give a melting point depression. The prepared acetophenone was also identified through the semicarbazone whose m.p. of 198-199° agreed with that of acetophenone semicabazone (198-200°).

Yield of acetophenone 2.1 g or 75% of the theoretical calculated on phenyltrichlorosilane. Yield of semicarbzone 81% of the theoretical, calculated on the acetophenone.

c) Preparation of phenyldichlorophosphine. 20.0 g (0.094 mole) phenyltrichlorosilane and 13.9 g (0.104 mole) anhydrous, freshly sublimed aluminum chloride were put into a round-bottomed flask connected to a reflux condenser and a receiver cooled with acetone-carbon dioxide mixture (−40°) and fitted with a calcium chloride tube. When the reactants were stirred, the mass turned red. The reaction was speeded up by heating for 10 hours at 70-80° with simultaneous removal of the silicon tetrachloride formed (the whole system was connected to a vacuum). In the receiver was collected 13.9 g $SiCl_4$ or 87% of the theoretical.

To the brown semisolid residue remaining after removal of the $SiCl_4$ was added stepwise 13.0 g (0.094 mole) phosphorous trichloride. After the addition the mixture became liquid. It was heated for an hour at 80-90°, and then addition was made (gradually) of 17.2 g (0.112 mole) phosphorous oxychloride (as a complexing agent for removal of $AlCl_3$), which led to formation of a granular precipitate.

The precipitate was treated with several portions of petroleum ether, the extracts were combined, the petroleum ether distilled off and the residue distilled in vacuum to give 12.8 g (70% of the theoretical) phenyldichlorosilane in the form of a highly refractive light yellow liquid with b.p. 140-141° at 57 mm, fuming in the air and possessing a sharp unpleasant odor.

Reaction of Diphenyldichlorosilane with $AlCl_3$

a) Preparation of benzene and phenyltrichlorosilane. A mixture (prepared with cooling) of 7.0 g (0.027 mole) diphenyldichlorosilane and 4.1 g (0.03 mole) freshly sublimed aluminum chloride was stood for 4 hours at 30-35°. The mass acquired a dark-red color. The cooled (to −30°) mass was treated with water (acidified with sulfuric acid) and distilled with steam. The benzene layer on the surface of the aqueous distillate was extracted with ether and dried over calcium chloride. After distilling off the ether, the residue (benzene) was distilled on the water bath to give 0.8 g liquid with b.p. 78-80° and d_4^{20} 0.880. Yield of benzene 38.0% of the theoretical calculated on the diphenyldichlorosilane.

The residue in the distillation flask (2.2 g), after steam distillation, consisted of a light-yellow, transparent resin whose analysis for silicon corresponded to that of the resin prepared from phenyltrichlorosilane. Silicon found: 21.3%; required 21.7%.

The yield of phenyltrichlorosilane, based on the amount of separated resin, was 65% of the theoretical calculated on the amount of diphenyldichlorosilane taken for the reaction.

b) Preparation of benzene and $SiCl_4$. To 8.0 g (0.032 mole) diphenyldichlorosilane was added (with cooling) 8.5 g (0.064 mole) aluminum chloride. The mixture was stood for 72 hours at 30-35°. The reaction mass had a dark-red color.

The liquid mass was carefully distilled in vacuum on a water bath. In the receiver, cooled with acetone-carbon dioxide mixture (−60°) collected a liquid with b.p. 56-57° and a pungent odor, resembling in boiling pt. and density (d_4^{20} 1.4841) silicon tetrachloride. Yield 3.3 g or 60% of the theoretical.

The semisolid brown residue after distillation of the $SiCl_4$ was decomposed with cold water. Appropriate treatment (see above) gave a liquid with a b.p. 79-80° whose density (d_4^{20} 0.876) also identified it as benzene. Yield 3 g or 61.2% of the theoretical.

Reaction of p-Chlorophenyltrichlorosilane* with $AlCl_3$.

a) Preparation of chlorobenzene. To 5.0 g (0.02 mole) p-chlorophenyltrichlorosilane was added 2.67 g (0.02 mole) aluminum chloride. The mixture turned red when stirred. It was left for 48 hours at room temperature and then carefully decomposed with water while cooling (−50°). Working-up as before (see preceding experiments) gave a liquid with b.p. 130-132°. The b.p. and density (d_4^{20} 1.1071) agreed with those of chlorobenzene. Yield 1.3 g or 56.5% of the theoretical. For further identification the prepared chlorobenzene was converted with nitrating mixture into a crystalline substance with m.p. 82.6° after recrystallization from alcohol and drying. This is the m.p. of p-chloronitrobenzene. Yield 75% of the theoretical, calculated on the chlorobenzene.

b) Preparation of p-chloroacetophenone. To 2.8 g (0.011 mole) p-chlorophenyltrichlorosilane was added 1.5 g (0.011 mole) aluminum chloride. The mixture stood for 24 hours at room temperature, after which 0.9 g acetyl chloride was added in the cold. After the mixture had been heated at 70-80° for 20 minutes, it was carefully decomposed (cooling at −30°) with iced water. The resultant oil partly crystallized on standing. After suitable treatment (see above details for acetophenone) crystals were obtained which, after recrystallization from alcohol had m.p. 19.6° (p-chloroacetophenone melts at 20°). Found chlorine 22.7%; required 22.9%. Yield 0.9 g or 53% of the theoretical. The prepared p-chloroacetophenone was identified as the oxime whose m.p. of 96° corresponded to that of p-chloroacetophenone oxime (95°). Yield of oxime 60% of the theoretical.

c) Preparation of p-chlorophenyldichlorophosphine. 10.0 g (0.04 mole) p-chlorophenyltrichlorosilane was stirred with 6.0 g (0.045 mole) freshly sublimed aluminum chloride and 5.7 g (0.041 mole) phosphorus trichloride. The mixture was heated for 2 hours on a water bath at 80°, after which the $SiCl_4$ was distilled off (6.3 g or 90.7% of the theoretical), and to the residue was gradually added 7.0 g (0.045 mole) phosphorus oxychloride. Isolation of $p\text{-}C_6H_4ClPCl_2$ was effected on the same lines as for $C_6H_5PCl_2$ (see above). There was obtained 6.6 g p-chlorophenyldichlorophosphine in the form of a colorless oily liquid with an unpleasant odor, b.p. 252-253°, d_4^{20} 1.4203. Yield 77.4% of the theoretical, calculated on the p-chlorophenyltrichlorosilane.

Reaction of p-Bromophenyltrichlorosilane with $AlCl_3$

Preparation of p-bromophenyldichlorophosphine. 10.0 g (0.034 mole) p-bromophenyltrichlorosilane** was stirred with 5.0 g (0.037 mole) aluminum chloride and 4.7 g (0.034 mole) phosphorus trichloride. The mixture was heated for 2 hours on a water bath at 80° following which the $SiCl_4$ was distilled off (5.2 g or 89.6% of the theoretical) and to the residue was gradually added 5.9 g (0.038 mole) phosphorus oxychloride. The $p\text{-}C_6H_4BrPCl_2$ was isolated by the same procedure as before (see preceding experiment). There was obtained 6.4 g p-bromophenyldichlorophosphine in the form of a colorless strongly refractive viscous liquid with b.p. 270°, d_4^{20} 1.6861. Yield 72.6% of the theoretical calculated on p-bromophenyltrichlorosilane taken in the reaction.

Reaction of (p-Chlorophenyl) phenyldichlorosilane with $AlCl_3$.

A mixture of 5.0 g (0.017 mole) (p-chlorophenyl) phenyldichlorosilane*** and 2.5 g (0.019 mole) freshly sublimed $AlCl_3$ was stood for 5 hours at 30-35° following which it was treated under cooling (−30°) with water acidified with sulfuric acid and distilled with steam. Working-up as in the preceding experiments gave a liquid with b.p. 131-132° identical in b.p. and density (d_4^{20} 1.1074) with chlorobenzene. Yield 1.0 g or 50% of the theoretical.

The residue in the flask (1.3 g) was steam distilled to give a yellow resin whose analysis for silicon corresponded to that of the resin prepared from phenyltrichlorosilane. Silicon found: 21.2%; required 21.7%.

The yield of phenylsilsesquioxane as resin was 57% of the theoretical calculated on the (p-chlorophenyl) phenyldichlorosilane taken in the reaction.

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* Prepared by reaction of p-chlorophenyl magnesium bromide with $SiCl_4$.

** Prepared by reacting p-bromophenyl magnesium bromide with $SiCl_4$.

*** Prepared from p-chlorophenyl magnesium bromide and phenyltrichlorosilane.

SUMMARY

1. A study was made of the reaction of $AlCl_3$ with phenyltrichlorosilane, diphenyldichlorosilane and their derivatives: p-chloro- and p-bromophenyltrichlorosilanes and (p-chlorophenyl)-phenyldichlorosilane. The effects of ratios of reactants (chlorosilane and $AlCl_3$) and of the presence of substituents in the aromatic nucleus on the course and results of these reactions were investigated.

2. It was shown from the transformations of the products of reaction of arylchlorosilanes with $AlCl_3$ that the intermediate products in these reactions are the corresponding organoaluminum compounds.

3. The action of acetyl chloride and PCl_3 on the intermediately formed organoaluminum compounds gives good yields of arylalkyl ketones and aryldichlorophosphines containing substituents such as chlorine and bromine in the nucleus.

4. The possibility is noted of using the reactions of arylchlorosilanes and their derivatives with $AlCl_3$ for syntheses of various organoelement compounds on the same lines as the described syntheses of phosphines.

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SYNTHESIS AND PROPERTIES OF SOME- α-NAPHTHYL-AMINO- AND α-NAPHTHYLAMINOPHENYLSILANES

V. S. Chugunov

In our previous investigations [1,2] were reported organomagnesium and -lithium syntheses of various organosilicon compounds containing α-naphthyl radicals. We thus prepared for the first time the following types of organosilicon compounds: $ArSiR_3$, Ar_2SiR_2 and Ar_3SiR, where $Ar = \alpha\text{-}C_{10}H_7$, and $R = OC_2H_5$, n.-C_4H_9 and C_6H_5.

Those investigations had established that reaction of α-naphthyl magnesium bromide with tetraethoxysilane only results in addition of two α-naphthyl radicals to the silicon atom, due to presence of considerable steric hindrances inherent in the α-naphthyl radical. When magnesium is replaced by lithium, the addition only proceeds up to the formation of tri-α-naphthylethoxysilane. For the above reason, tetra-α-naphthylsilane is not formed even when silicon tetrachloride is boiled in ether with excess of α-naphthyllithium. In these conditions the reaction comes to an end with formation of only tri-α-naphthylchlorosilane [3]. It is interesting to note that the α-naphthyl radical containing a substituent in the second benzene ring, say in the para-position, in similar synthesis conditions forms tetra-α-naphthylsilane in very good yield (81%) [4]. It was also established that α-naphthyl-n-butysilane and di-α-naphthyldi-n-butylsilane are obtained in up to 60% yields via the organolithium and -magnesium compounds, whereas tri-α-naphthyl-n-butylsilane was obtained in only 22% yield when starting from tri- α-naphthylchlorosilane and n-butyllithium [3].

Concerning the synthesis of α-naphthyltriphenylsilane, it must be noted that we prepared it by reacting α-naphthyltriethoxysilane with excess of phenyl magnesium bromide, whereas its corresponding hydrocarbon — α-naphthyltriphenylmethane could not be prepared by the organomagnesium synthesis; as we know, in these conditions the α-naphthyldiphenylmethyl free radical is formed [5]. Di-α-naphthyldiphenyl- and tri-α-naphthylphenylsilanes were obtained in lower yields (60 to 27%) with the help of organolithium compounds.

In the present investigation, starting from the corresponding α-naphthylfluorosilanes, the aim was to prepare α-naphthylamino- and α-naphthylaminophenylsilanes and to clarify their physicochemical properties. The composition and properties of the starting materials as well as of the compounds now synthesized by us for the first time are set forth in the table.

Physicochemical Properties, Reaction Components and Yields of α-Naphthylfluoro-, amino- and -aminophenylsilanes.

Name of Substance	M.p.	Reaction Components	Yields (%)	Literature References
α-Naphthyltrifluorosilane	Liquid	$C_{10}H_7MgBr + SiF_4$	—	[6]
Di-α-naphthyldifluorosilane	79-81°	$C_{10}H_7MgBr + SiF_4$	22	[6]
Tri-α-Naphthylfluorosilane	226-227	$C_{10}H_7MgBr + SiF_4$	26	[7]
α-Naphthylaminosilane	—	$C_{10}H_7SiF_3 + NH_3$	—	Unstable
Di-α-naphthyldiaminosilane	154-156	$(C_{10}H_7)_2SiF_2 + NH_3$	Quantitative	Prepared by us
Tri-α-naphthylaminosilane	204-206	$(C_{10}H_7)_2SiF + NH_2Na$	50	Prepared by us
α-Naphthyltriaminophenysilane	176-179	$C_{10}H_7SiF_3 + C_6H_5NH_2$	Quantitative	Prepared by us
Di-α-naphthyldiaminophenylsilane	184-186	$(C_{10}H_7)SiF_3 + C_6H_5NH_2$	72	Prepared by us
Tri-α-naphthylaminophenylsilane	198-200	$(C_{10}H_7)_3SiF + C_6H_5NHNa$	27	Prepared by us

The starting α-naphthylfluorosilanes listed in the table were prepared by passing into an ethereal solution of α-naphthyl magnesium bromide a stream of silicon fluoride prepared from sodium fluosilicate and concentrated sulfuric acid in presence of finely pulverized glass powder; depending on the molar ratios of silicon fluoride to α-bromo-naphthyl magnesium and on the reaction temperature, there is formed either α-naphthyltrifluorosilane in admixture with di-α-naphthyldifluorosilane or only tri-α-naphthylfluorosilane.

In α-naphthylfluorosilanes depending on the number of sterically hindering α-naphthyl radicals attached to the silicon atom, the replacement of fluorine by hydroxyl, amino or aminophenyl groups proceeds at varying velocities. Thus, whereas in α-naphthyltrifluorosilane the fluorine is quickly hydrolyzed by acidified water even in the cold, in di-α-naphthyldifluorosilane the fluorine is quite stable even in 50% acetic acid.

The fluorine is particularly firmly combined in tri-α-naphthylfluorosilane in which it is hydrolyzed with difficulty by hot 20-25% NaOH solution.

These factors lead to α-naphthylfluorosilanes in question reacting at different rates with ammonia gas and aniline. When ammonia, for example, is passed into an ethereal solution of α-naphthyltrifluorosilane, heat is developed and a flocculent precipitate is formed, evidently a mixture of α-naphthylaminosilanes which are easily hydrolyzed by moist air to form resinous polymers. But the replacement of fluorine in di-α-naphthyldifluorosilane by the amino group takes place even on heating the ethereal solution with formation of di-α-naphthylaminosilane, which is quite stable to moisture. This compound melts at 154-156° and solidifies to a vitreous mass. In tri-α-naphthylfluorosilane, the fluorine is replaced with difficulty only after prolonged boiling in toluene with excess of sodamide. The resultant tri-α-naphthyaminosilane is an amorphous substance melting at 202-204°. The only analog reported in the literature, triphenylaminosilane, melts at 55-56° [8].

Concerning α-naphthylaminophenylsilanes, here also α-naphthyltriaminophenylsilane is formed more easily; by heating of α-naphthyltrifluorosilane in toluene to 60-70° with excess of aniline, it is formed in quantitative yield. On the other hand, the formation of di-α-naphthyldiaminophenylsilane requires prolonged boiling. Tri-α-naphthylaminophenylsilane is formed in 27% yield only after boiling tri-α-naphthylfluorosilane for 6 hours in toluene with excess of sodium anilide.

EXPERIMENTAL

The starting substances were α-naphthyltrifluoro di-α-naphthyldifluoro- and tri-α-naphthylfluorosilanes, prepared [6, 7] by passing the appropriate amounts of $SiCl_4$ into an ethereal solution of α-naphthyl magnesium bromide.

α-Naphthyltriaminosilane $\alpha\text{-}C_{10}H_7Si(NH_2)_3$. Dry ammonia was passed for 30 minutes into a solution of 6.0 g α-naphthyltrifluorosilane in 50 ml absolute ether. Heat was developed and an abundant amorphous precipitate came down. In contact with moist air it rapidly hydrolyzes with evolution of ammonia and formation of a resin (soluble in organic solvents) which burns with a smoky flame and leaves a residue of silica.

Di-α-naphthyldiaminosilane $(\alpha\text{-}C_{10}H_7)_2Si(NH_2)_2$. A stream of dry ammonia was passed into a solution heated to 30-33° of 8.0 g di-α-naphthyldifluorosilane in 50 ml ether for 1 hour. The precipitate was filtered off and twice recrystallized from pyridine. Yield 7.6 g di-α-naphthyldiaminosilane in the form of a fine, colorless powder, melting at 154-156° and solidifying to a vitreous mass with a light-yellow color.

Found % Si 8.6, 8.4; N 8.6. $C_{20}H_{18}SiN_2$. Calculated % Si 8.9; N 8.9.

Tri-α-naphthylaminosilane $(\alpha\text{-}C_{10}H_7)_3SiNH_2$. To 8.5 g tri-α-naphthylfluorosilane dissolved in 50 ml toluene was added 6.0 g freshly prepared sodamide [9]. With precautions against entry of moisture from the air, the solution was boiled for 6 hours; the flocculent precipitate of sodium fluoride was filtered off. Three crystallizations from toluene gave 4.2 g tri-α-naphthylaminosilane as a fine, colorless powder, melting at 204-206° and about 3 g unreacted tri-α-naphthylfluorosilane.

Found % Si 6.1, 6.0; N 3.2, 3.1. $C_{30}H_{23}SiN$. Calculated %: Si 6.5; N 3.2.

α-Naphthyltriaminophenylsilane $\alpha\text{-}C_{10}H_7Si(NHC_6H_5)_3$. To 6.5 g α-naphthyltrifluorosilane dissolved in 50 ml toluene was added 9.5 g freshly distilled aniline and the solution was heated for an hour at 60-70°. After removal of the aniline hydrofluoride, the product was recrystallized from toluene to give 12.2 g α-naphthyltriaminophenylsilane, melting at 176-178° and solidifying to a vitreous mass.

Found % Si 6.2, 5.9; N 11.5, 11.6. $C_{28}H_{25}SiN_3$. Calculated %: Si 6.5; N 11.2.

Di-α-naphthyldiaminophenylsilane $(\alpha\text{-}C_{10}H_7)_2Si(NHC_6H_5)_2$. 6.5 g di-α-naphthyldifluorosilane and 8 g freshly distilled aniline were boiled in 50 ml toluene for 5 hours. Removal of the toluene-insoluble precipitate was followed by separation of 6.7 g fine powder of di-α-naphthyldiaminophenylsilane, melting at 184-186° and solidifying to a vitreous mass.

Found %: Si 6.3, 5.8; N 6.2, 6.4. $C_{34}H_{28}SiN_2$. Calculated %: Si 6.0; N 6.0.

Tri-α-naphthylaminophenylsilane $(\alpha\text{-}C_{10}H_7)_3SiNHC_6H_5$. To a freshly prepared solution of sodium anilide prepared by boiling 8 g aniline for 4 hours with excess sodium in 50 ml toluene, was added 8.5 g tri-α-naphthylfluorosilane,

and the solution was again boiled for 6 hours. Removal of the sodium fluoride was followed by isolation from the solution of 2.7 g tri-α-naphthylaminophenylsilane, melting at 198-200°, and about 4 g of unreacted tri-α-naphthylfluorosilane.

Found %: Si 5.3, 5.1; N 2.8, 2.5. $C_{36}H_{27}SiN$. Calculated %: Si 5.6; N 2.8.

SUMMARY

1. The fluorine in α-naphthyltrifluoro- and di-α-naphthyldifluorosilanes can be readily replaced by the amino or aminophenyl group by the action of ammonia or aniline.

2. The fluorine of tri-α-naphthylfluorosilane can only be replaced by boiling the compound in toluene with excess of sodamide or sodium anilide.

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STERIC HINDRANCES IN ORGANOMAGNESIUM REACTIONS

XVI. PREPARATION OF KETONES BY REACTION OF ACID CHLORIDES WITH ORGANOMAGNESIUM COMPOUNDS

I. I. Lapkin

Continuing the study of the method for preparing ketones based on reaction of acid chlorides with organomagnesium compounds [1,2], we set out to establish the possibility of synthesizing alkoxyl-containing ketones by this method.

As we know, the application of the Gustavson-Friedel-Crafts method to the preparation of such ketones is not always successful due to the cleaving action of aluminum chloride on alkoxyl groups.

Although Fuson and his co-workers [3,4,5] showed that the Grignard reagent sometimes reacts with methoxybenzonitrile with substitution of the methoxyl group by the radicals of the organomagnesium compounds, this substitution was not observed in a single case in the experimental conditions of our own investigation.

Our results are set forth in the table.

The data of the table fully confirm those characteristics of the course of the reaction between organomagnesium compounds and acid chlorides that we had established in previous investigations [1,2]; they also provide evidence that the method in question is highly suitable for the synthesis of alkoxyl-containing ketones.

EXPERIMENTAL

(In collaboration with L. G. Bilgildeeva, A. A. Vyatkina, V. Ya. Vlasova, G. V. Shilova and G. V. Maksimova)

1. Reaction of β-methoxy-α-naphthyl magnesium bromide with benzoyl chloride (1:1 ratio). Reactants: 29.6 g ($\frac{1}{8}$ mole) α-bromo-β-methoxynaphthalene, 4 g magnesium and 17.5 g ($\frac{1}{8}$ mole) benzoyl chloride.

Since β-methoxy-α-naphthyl magnesium bromide is relatively poorly soluble in absolute ether, it was synthesized in a mixture of ether and toluene (1:1). To the benzoyl chloride dissolved in toluene was added dropwise, with cooling and stirring, the ether-toluene solution of β-methoxy-α-naphthyl magnesium bromide. The mixture was heated for an hour. In order to avoid cleavage of the methoxyl group under the action of hydrochloric acid, saponification of the residual acid chloride was effected not with water but with 10% sodium carbonate solution. Heating with sodium carbonate was carried out for 30 minutes. The ether-toluene layer was separated from the aqueous layer, washed with water until neutral, and dried with sodium sulfate.

The mixture of compounds remaining behind after distilling off the solvent was distilled in vacuum. A second distillation of the main fraction (220-280° at 8 mm) gave 11 g of phenyl-(β-methoxy-α-naphthyl) ketone (34% yield). B.p. 240-242° at 7 mm, m.p. 125-126° (from ligroin).

0.1390 g substance: 0.4190 g CO_2, 0.0670 g H_2O. 0.1398 g substance: 0.1170 g AgI. Found %: C 82.26; H 5.39; OCH_3 11.06. $C_{18}H_{14}O_2$. Calculated %: C 82.42; H 5.38; OCH_3 11.83.

An increase in the amount of organomagnesium compound to a 2:1 ratio brought the yield of ketone to 68%.

In the literature [6] the m.p. of phenyl-(β-methoxy-α-naphthyl)-ketone is given as 125°.

2. Reaction of β-ethoxy-α-naphthyl magnesium bromide with benzoyl chloride (2:1 ratio). The reactants were 31.1 g ($\frac{1}{8}$ mole) α-bromo-β-ethoxynaphthalene, 4 g magnesium and 8.8 g ($\frac{1}{16}$ mole) benzoyl chloride.

Reaction conditions were the same as in the preceding experiment except that the order of mixing of the components was changed, the ethereal solution of benzoyl chloride being added to the ethereal solution of the organomagnesium compound.

TABLE

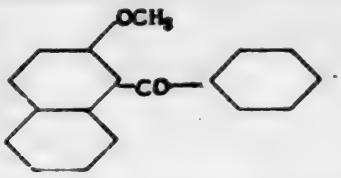
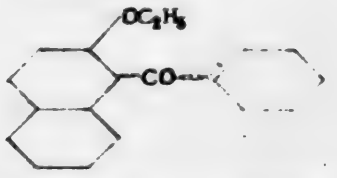
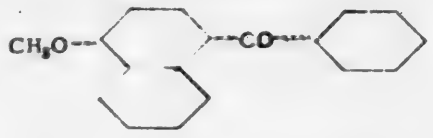
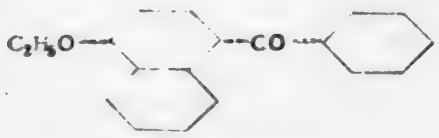
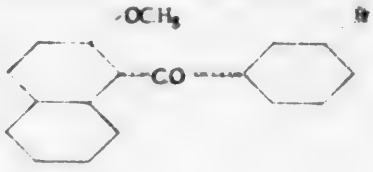
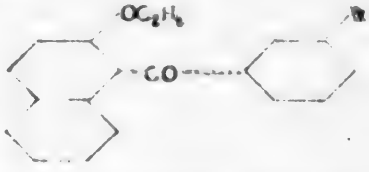
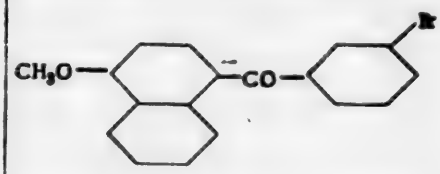
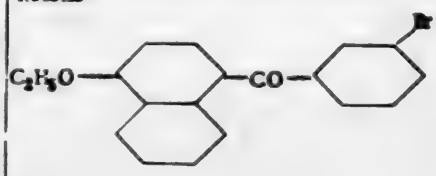
Prep. No.	Reaction components	Ratio of components	Formula of ketone	Yield of ketone (%)
1	β-Methoxy-α-naphthyl magnesium bromide + benzoyl chloride	1:1	 Phenyl-[β-methoxy-α-naphthyl]-ketone	34
2	The same	2:1	The same	68
3	β-Ethoxy-α-naphthyl magnesium bromide + benzoyl chloride	2:1	 Phenyl-[β-ethoxy-α-naphthyl]-ketone	70
4	4-Methoxy-1-naphthyl magnesium bromide + benzoyl chloride	1:1	 Phenyl-[4-methoxy-1-naphthyl] ketone	52
5	4-Ethoxy-1-naphthyl magnesium bromide + benzoyl chloride	1:1	 Phenyl-[4-ethoxy-1-naphthyl] ketone	50
6	β-Methoxy-α-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[β-methoxy-α-naphthyl] ketone	48
7	β-Ethoxy-α-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[β-ethoxy-α-naphthyl]-ketone	50

TABLE (continued)

Prep. No.	Reaction components	Ratio of components	Formula of ketone	Yield of ketone (%)
8	4-Methoxy-1-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[4-methoxy-1-naphthyl]-ketone	55
9	4-Ethoxy-1-naphthyl magnesium bromide + m-bromobenzoyl chloride	1:1	 m-Bromophenyl-[4-ethoxy-1-naphthyl]-ketone	56

Phenyl-(8-ethoxy-α-naphthyl) ketone was isolated in the amount of 12 g (70%). B.p. 211-212° at 2 mm; m.p. 79-80° (from ligroine).

0.1406 g substance: 0.4242 g CO_2; 0.0710 g H_2O; 0.1572 g substance: 0.1708 g AgI. Found %: C 82.72; H 5.65; OC_2H_5 14.4. $C_{19}H_{16}O_2$. Calculated %: C 82.58; H 5.83; OC_2H_5 16.3

This ketone has not been described in the literature.

3. Reaction of 4-methoxy-1-naphthyl magnesium bromide with benzoyl chloride (1:1) ratio. Starting materials: 35.5 g (1/6 mole) 1-bromo-4-methoxynaphthalene, 5 g magnesium and 23.4 g (1/6 mole) benzoyl chloride.

Reaction conditions were as in the first experiment.

The main fraction (220-240° at 7 mm) weighed 26 g. A second distillation of the main fraction gave 23 g (52%) phenyl (4-methoxy-1-naphthyl)-ketone. B.p. 213-215° at 4 mm; m.p. 81-82° (from a mixture of ligroine and toluene).

0.1136 g substance: 0.3425 g CO_2; 0.0530 g H_2O. 0.1252 g substance: 0.1065 g AgI. Found %: C 82.27; H 5.22; OCH_3 11.24. $C_{18}H_{14}O_2$. Calculated %: C 82.42; H 5.38; OCH_3 11.83.

In the literature the m.p. of this ketone [7] is given as 82-83°.

4. Reaction of 4-ethoxy-1-naphthyl magnesium bromide with benzoyl chloride (1:1 ratio). Starting substances: 41.8 g (1/6 mole) 1-bromo-4-ethoxynaphthalene, 5 g magnesium and 23.4 g (1/6 mole) benzoyl chloride.

The mixture of substances obtained in the reaction (carried out under the conditions of the first experiment) was distilled in vacuum at 8 mm. First fraction to 215°; second fraction 215-260°, 25 g; residue in flask 3 g. A second distillation of the second fraction gave 23 g (50%) phenyl-(4-ethoxy-1-naphthyl)-ketone. B.p. 245-247° at 8 mm; m.p. 71-72° (from ligroine + toluene).

0.0955 g substance: 0.3004 g CO_2; 0.0511 g H_2O. 0.1335 g substance: 0.1099 g AgI. Found %: C 82.37; H 5.74; OC_2H_5 16.16. $C_{19}H_{16}O_2$. Calculated %: C 82.58; H 5.83; OC_2H_5 16.30.

Phenyl-(4-ethoxy-1-naphthyl)ketone has a m.p. of 74-75° according to the literature [8].

5. Reaction of β-methoxy-α-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio). The amounts of starting materials were each 1/8 mole.

Reaction conditions were as in the first experiment.

The yield of m-bromophenyl-(β-methoxy-α-naphthyl)-ketone was 48% (20.5 g). B.p. 250-253° at 6 mm; m.p. 99-100° (from ligroine).

0.1565 g substance: 4.6 ml 0.1N $AgNO_3$. 0.2404 g substance: 0.1550 g AgI. Found %: Br 23.49 (Stepanov's method), OCH_3 8.5. $C_{18}H_{15}O_2Br$. Calculated %: Br 23.42; OCH_3 9.1.

m-Bromophenyl-(β-methoxy-α-naphthyl)-ketone forms a picrate with m.p. 114-115°.

0.0445 g substance: 2.3 ml 0.1 N HCl (hydrogenation by Ter Meulen method). Found %: N 7.24. $C_{24}H_{18}O_9N_3Br$. Calculated %: N 7.36.

Neither the ketone nor its picrate are mentioned in the literature.

6. Reaction of β-ethoxy-α-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio). Starting materials in amounts of 1/8 mole each.

m-Bromophenyl-(β-ethoxy-α-naphthyl)-ketone partly decomposes when distilled in vacuum; after removal of solvent it was therefore isolated from the reaction mixture by freezing. M.p. 97-98° (from ligroine). Yield 22 g (50%).

0.1811 g substance: 5.1 ml 0.1 N $AgNO_3$ (Stepanov's method). 0.1529 g substance: 0.0948 g AgI. Found %: Br 22.50, OC_2H_5 11.91. $C_{19}H_{15}O_2Br$. Calculated %: Br 22.50; OC_2H_5 12.68.

This ketone is likewise not described in the literature.

7. Reaction of 4-methoxy-1-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio). Reaction components were 34.0 g (1/7 mole) 1-bromo-4-methoxynaphthalene, 5 g magnesium and 31.3 g (1/7 mole) m-bromobenzoyl chloride.

Vacuum distillation (8 mm) of the reaction product gave the following fractions: I) up to 205°; II) 205-206°. 30 g residue in flask 1 g. A second distillation of the second fraction gave 27 g (55%) of m-bromophenyl-(4-methoxy-1-naphthyl)-ketone. B.p. 244-245° at 5 mm; m.p. 129° (from ligroine-toluene mixture).

0.1001 g substance: 0.0546 g AgBr. 0.0814 g substance: 2.3 ml 0.1 N $AgNO_3$. Found %: Br 23.20; OCH_3 8.8. $C_{19}H_{15}O_2Br$. Calculated %: Br 23.42; OCH_3 9.1.

m-Bromophenyl-(4-methoxy-1-naphthyl)-ketone is not described in the literature.

8. Reaction of 4-ethoxy-1-naphthyl magnesium bromide with m-bromobenzoyl chloride (1:1 ratio). Starting substances 36.0 g (1/7 mole) 1-bromo-4-ethoxynaphthalene, 5 g magnesium and 31.3 g (1/7 mole) m-bromobenzoyl chloride.

The yield of m-bromophenyl-(4-ethoxy-1-naphthyl)-ketone was 28 g (56%). M.p. 95-96° (from ligroine-toluene mixture).

0.0967 g substance: 2.7 ml 0.1 N $AgNO_3$ (Stepanov's method). 0.1033 g substance: 2.8 ml 0.1 N $AgNO_3$ (Kürpal method). Found %: Br 22.28; OC_2H_5 12.21. $C_{19}H_{15}O_2Br$. Calculated %: Br 22.50; OC_2H_5 12.68.

This ketone has not previously been reported in the literature.

SUMMARY

1. The research described in this paper demonstrates the possibility of synthesis of ketones by the reaction of organomagnesium compounds with acid chlorides, even in more complicated cases when the reactants contain various alkoxyl groups.

2. 8 Alkoxyl-containing ketones have been synthesized, of which 5 have not previously been described in the literature.

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*See Consultants Bureau Translation, p. 677.

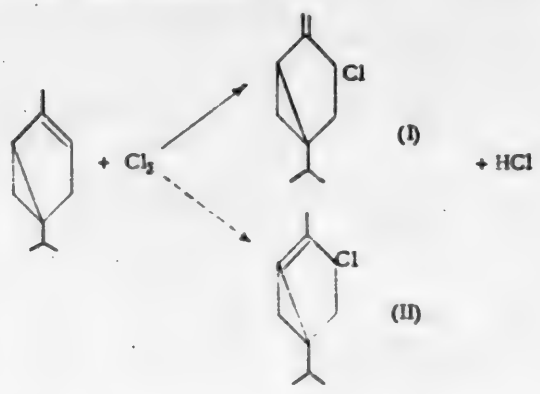
**See Consultants Bureau Translation, p. 1411.

NEW TYPES OF TERPENE TRANSFORMATIONS

XIII. THE ACTION OF CHLORINE ON α-THUJENE

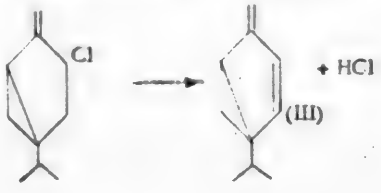
D. Tishchenko and T. Danilova

In Communication I general consideration was given to the characteristics of reaction of chlorine with terpenes [1], while in Communication V experimental data were presented for the action of chlorine on Δ^3-carene. It was found that in our chosen conditions the three-membered ring of carene does not react either with chlorine or with hydrogen chloride, and the primary product of the reaction is 3-chloro-Δ^4-carene. It was desirable to establish whether this case of stability of the three-membered ring in bicyclic terpenes was the rule or an exception. To this end we studied the action of chlorine on α-thujene. α-Thujene is an analog of trimethylethylene, and hence Lvov's reaction should proceed for it with a sufficiently high yield, although lower than for trimethylethylene (about 90%), due to the "hemicyclic prohibition"; another direction of the reaction is improbable due to the "Bredt prohibition."



Chloride (I) should be stable at 70°, and on ozonization it should give formaldehyde (or formic acid) and a chloroketone of the composition $C_9H_{15}OCl$. Chloride (II) on ozonization will give a chlorodiketone $C_{10}H_{15}O_2Cl$. Ozonization gave a chloroketone, thus establishing structure (I) for the chloride of α-thujene (3-chlorosabinene). Cleavage by chlorine of the three-membered ring should give a monochloride with two double bonds, which would exclude the possibility of obtaining the chloroketone $C_9H_{15}OCl$. It was thus shown that the case of Δ^3-carene is not exceptional and that the three-membered ring in bicyclic terpenes is stable in our chosen chlorination conditions.

We brought chloride (I) into reaction with potassium acetate; apart from the expected ester of terpenol, there was obtained a substance which was brightened both as vapor and liquid and whose constants corresponded to a hydrocarbon $C_{10}H_{14}$ ("dehydroterpene"). We obtained these "dehydroterpenes" by removing a molecule of hydrogen chloride from the monochlorides of terpinolene, carene and β-pyronene. In composition they correspond to tetramethylbenzenes and other isomers of aromatic hydrocarbons of the composition $C_{10}H_{14}$, but they differ conspicuously from the latter in physical and chemical properties. The latter three "dehydroterpenes" are colorless; the "dehydroterpene" from 2-chlorosabinene is colored, which fact is fully consistent with its most probable structure (III):



Dimethylfulvene

This structure of 2,7-sabinadiene emphasizes its analogy with the colored fulvenes, hydrocarbons with a crossed system of conjugated double bonds, if we assume that it contains a three-membered ring without a multiple bond. The other possible structure of 1,7-sabinadiene with an allenic grouping is very much less probable both from thermodynamic considerations and from the fact that our "dehydroterpene" is colored. Allenic hydrocarbons are colorless. We established that the "dehydroterpene" from terpinolene chloride corresponds to the structure 1,3,8(9)-p-menthatriene, and the "dehydroterpene" from carene chloride to 2,4-caradiene. They are both isomeric with 2,7-sabinadiene, and of course with p-cymene, and their isomerization to p-cymene ought to be accompanied by very considerable release of energy ("ring aromatization"). This isomerization, however, does not take place either on formation of "dehydroterpenes" or during their isolation and purification. These facts throw doubt on the now fairly widespread views of the structure of systems of conjugated double bonds. The theory is that in such systems the valence electrons are not firmly anchored between the respective atoms and can move fairly freely throughout the whole system, "creating a different density of electron cloud at different points". Such a "mobility of the electron cloud" should greatly facilitate, thermochemically, advantageous isomerization reactions, as in our case for instance. In actual fact, "dehydroterpenes" are fairly stable. We are forced to the conclusion that the ideas about "mobility of the electron cloud in a system of conjugated double bonds", in our case at least, do not accord with the facts.

We did not prove the structure of terpenol, prepared by reaction of potassium acetate with 2-chlorosabinene. It can be either 2-hydroxysabinene or 7-hydroxy-α-thujene (allyl rearrangement in the instant of the ion-exchange reaction).

This investigation showed that the mechanism of reaction with chlorine advanced by us in Communication I is also valid for α-thujene, that the resultant 2-chlorosabinene may be brought into anion exchange reaction to give the corresponding derivatives and that by cleavage of a molecule of hydrogen chloride it is converted into an orange-colored "dehydroterpene", a hydrocarbon with the composition $C_{10}H_{14}$, apparently 2,7-sabinadiene.

EXPERIMENTAL

α-Thujene was prepared by Chugaev's method [2] from DL-thujyl alcohol, which we obtained from β-thujone by reduction with isopropyl alcohol in presence of aluminum isopropylate [4]. Rectification of the mixture of hydrocarbons in a column with an efficiency of 40 theoretical plates yielded a constant boiling fraction identified as α-thujene with b.p. 49-50° at 21 mm.

d_4^{18} 0.829 n_D^{18} 1.4512; MR_D 44.22. $C_{10}H_{16}$. $^F\Delta$. Calculated 44.21.

Chlorination was performed in conditions which have often been described. Reagents were α-thujene 111 g, $KMnO_4$ 30 g, HCl (1:19) 120 ml, sodium bicarbonate 100 g. The organic products of reaction weighed 126.9 g and contained 18.46 g chlorine. The inorganic chlorine content was 10.11 g. per cent anomalous reaction = 70.8.

The reaction product was fractionated in a column of 6-7 theoretical plates and at a bath temperature not higher than 70°. The main fraction of monochloride had b.p. 37° at 0.17 mm.

d_4^{18} 0.984 n_D^{18} 1.4862. MR_D 49.78. $C_{10}H_{15}Cl$. $^F\Delta$. Calculated 49.08.

The exaltation of refraction (0.7) is exactly characteristic of the hemicyclic double bond conjugated with a three membered ring.

0.1424, 0.1704 g substance: 0.1132, 0.1372 g AgCl. Found %: Cl 19.7, 20.9. $C_{10}H_{15}Cl$. Calculated %: Cl 20.8. Allylic chlorine was found by digesting a weighed sample with potassium acetate in acetic acid: 19.3 and 19.3%.

Ozonization of the monochloride. 10 g monochloride in 80 ml chloroform was ozonized with 78 liters of 5% ozone. The chloroform was removed from a tenth part of the solution of the ozonide in vacuum. Residue was a viscous liquid weighing 1.3 g.

0.2014 g substance: 0.4026 g CO_2; 0.1298 g H_2O. 0.2203, 0.1418 g substance: 0.1472, 0.0960 g AgCl. Found %: C 54.5; H 7.2; Cl 16.5, 16.7. $C_{10}H_{15}O_3Cl$. Calculated %: C 54.9; H 6.9; Cl 16.2.

The remaining ozonide solution was hydrolyzed by slow addition to boiling water, while the hydrolysis products were distilled off. In the aqueous layer was found 0.6 mole formic acid and 0.3 mole formaldehyde (isolated as formal dimedone).

The chloroform was driven out of the chloroform layer; the weight of the residue was 6.5 g; it was fractionated at 0.1 mm. The principal fraction (3.9 g) melted at 86-88°.

d_4^{20} 1.105; n_D^{20} 1.4896; MR_D 45.1; $C_9H_{13}OCl$ Δ (chloroketone). Calculated: 44.94.

0.1197, 0.1272 g substance: 0.2731, 0.2908 g CO_2; 0.0852, 0.0916 g H_2O. 0.1015, 0.1747 g substance: 0.0800, 0.1392 g AgCl. Found %: C 62.2, 62.3; H 8.0, 8.1; Cl 19.5, 19.7. $C_9H_{13}OCl$. Calculated %: C 62.7; H 7.5; Cl 20.5.

Oxidation of the chloroketone. 0.9 g was oxidized with a solution of 0.2 g permanganate. The isolated crystalline acid with m.p. about 140° was transformed into the silver salt.

Found %: Ag 53.1, 52.6. $C_9H_{13}O_4Ag_2$. Calculated %: Ag 53.9.

Preparation of the semicarbazone. To a solution of 0.4g chloroketone in alcohol was added an aqueous solution of 0.4 g potassium acetate and 0.4 g semicarbazide hydrochloride. The resultant precipitate was dissolved in alcohol with heating. Crystals came down after 3 days and were washed in alcohol and dried. M.p. 220°; no chlorine present. Its analysis corresponded closest of all to the semicarbazido-semicarbazone $C_{11}H_{19}O_2N_6$.

Found %: N 27.5, 27.8. $C_{11}H_{19}O_2N_6$. Calculated %: N 31.3.

Reaction of 2-chlorosabinene with potassium acetate. 14.5 g monochloride, 13 g of the salt and 10 g acetic acid were heated 4 hours on a water bath and then 2 hours on a sand bath at the boil. After cooling, the solution was diluted with three times the volume of water and extracted with ligroine. In the aqueous layer was found 5.6 g chlorine; the reaction took place to the extent of 90%. The solvent was removed from the extract; weight of residue 15.4 g; it was fractionated in a small column and gave two main fractions: 1) b.p. 40-41° at 5 mm (yield about 30% of the possible); 2) b.p. 74.6° at 2 mm (yield about 30% of the possible).

Fraction 1) was a mobile, dark-orange liquid; the vapor had the same color:

d_4^{20} 0.855, n_D^{20} 1.4860; MR_D 45.5. $C_{10}H_{14}$ F_2 Δ. Calculated 43.75.

0.0632, 0.0534 g substance: 0.2080, 0.1752 g CO_2; 0.0655, 0.0556 g H_2O. Found %: C 89.7, 89.5; H 11.6, 11.7. $C_{10}H_{14}$. Calculated %: C 89.55, H 10.45.

The total % of C and H = 101.2. The combustion analysis for benzoic acid gave a systematic error for hydrogen of the order of + 0.6 to + 0.7%. With this correction the analytical figures are acceptable and correspond to the composition $C_{10}H_{14}$.

The hydrocarbon is decolorized when its benzene solution is heated with maleic anhydride.

Fraction 2) is colorless.

d_4^{20} 0.969; n_D^{20} 1.47065; MR_D 55.94. $C_{10}H_{15}OCOCH_3$ F Δ. Calculated: 55.10.

Saponification number, found 282, calculated 288.

Preparation of the alcohol. 2.5 g fraction 2) was heated on a bath for 2 hours with a solution of 1 g KOH in 50 ml alcohol. The reaction product had an orange color. The solution was diluted with three times the volume of water and extracted with ligroine. The solvent was driven off from the extract and the residue fractionated at 3 mm. The first runnings were colored orange ("dehydroterpene"); at 66-68° the anticipated terpenol came over (1.2g).

d_4^{20} 0.942; n_D^{20} 1.4861; MR_D 46.33. $C_{10}H_{16}O$ F Δ. Calculated 45.74.

Found%: OH 10.5, 10.7. (Chugaev-Tserevitinov). $C_{10}H_{16}O$. Calculated %: OH 11.2.

Semmler [3] gives for sabinol d_4^{15} 0.943; n_D^{15} 1.488.

SUMMARY

1. The action of chlorine on α-thujene was investigated.

2. In accord with the considerations developed in Communication I the main product of the reaction is 2-chlorosabinene.

3. Reaction of 2-chlorosabinene with potassium acetate leads to the ester of terpenol and dark-orange "dehydroterpene" $C_{10}H_{14}$, probably 2,7-sabinadiene, an analog of the fulvenes.

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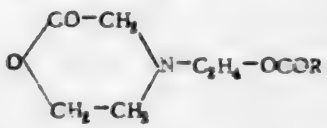
* See Consultants Bureau English translation, page 593.

SYNTHESIS AND TRANSFORMATIONS OF SOME DERIVATIVES OF N,N-DI-(β-HYDROXYETHYL)-AMINOACETIC ACID

II. ESTERS OF N,N-DIHYDROXYETHYLAMINOACETIC ACID AND N-HYDROXYETHYLMORPHOLONE

N. V. Khromov and A. L. Remizov

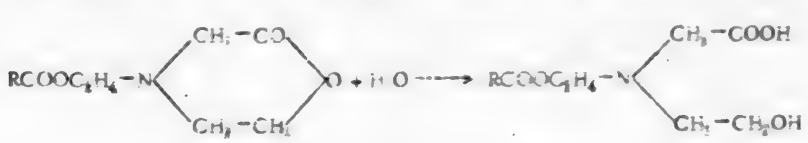
In the previous communication [1] it was pointed out that the dehydration of N,N-di-(β-hydroxyethyl)-aminoacetic acid in presence of hydrochloric acid leads to formation of the hydrochloride of N-(β-hydroxyethyl)-morpholone-2. Consistent with this structure of the compound is the complete identity of its acetyl, benzoyl and diphenylacetyl derivatives (esters) with the acetic (I), benzoic (II) and diphenylacetic (III) esters of N-hydroxyethylmorpholone synthesized from the latter when reacted in the form of the free base.



R = CH_3; C_6H_5; $(C_6H_5)_2CH$
(I) (II) (III)

Preparation of the esters both from the hydrochloride and from hydroxyethylmorpholone base was effected with the help of the acid chlorides of the corresponding acids in a medium of pyridine. None of the three esters is described in the literature. They are glycerol-like liquids with very weak basic properties. The hydrochlorides of the esters proved to be unstable (they deliquesced in the air and dissociated even when heated gently); they were therefore identified through the picrates and picrolonates. The picrate and picrolonate of acetate (I), the picrate of benzoate (II) and the picrolonate of diphenylacetate (III) were prepared for this purpose. The last-named ester had such feeble basic properties that it did not form a stable picrate. Even the picrolonate was distinguished by lability and decomposed on crystyllization.

In the same way as hydroxyethylmorpholone on hydrolysis gives dihydroxyethylaminoacetic acid, so also the synthesized cyclic esters on heating with water are transformed into the corresponding acids by the reaction:



R = CH_3 C_6H_5 $(C_6H_5)_2CH$
(IV) (V) (VI)

The acids (IV, V, VI) prepared in this way are monoesters of dihydroxyethylglycine; they are crystalline substances. During melting they lose water to form the original esters of hydroxyethylmorpholone; once melted, therefore, they do not solidify on cooling and in all their physical and chemical properties (solubility, formation of picrates and picrolonates) they become perfectly identical with the corresponding esters of hydroxyethylmorpholone.

In solutions containing water, both forms of the esters (the acidic and the lactone) apparently exist in equilibrium which with rising temperature is shifted in the direction of closure of the lactone ring, as can be conveniently observed in the case of the aqueous solution of the monobenzoate of dihydroxyethylglycine (V). This compound is notable for its high solubility in water, whereas the benzoate of hydroxyethylmorpholone (II) formed from it is almost insoluble in water. If the aqueous solution of the open-chain form is evaporated on the water bath to a very small volume and then diluted with water, the liquid separates into two layers: an upper one aqueous and a lower oily one. In all its properties the oil

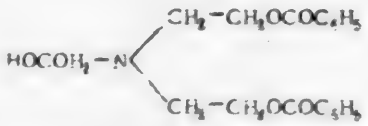
is identical with the benzoate of hydroxyethylmorpholone.

Consequently the process of opening of the lactone ring even proceeds in aqueous solutions. This is also demonstrated by the fact that after evaporation of the solvent (aqueous methanol or ethanol) from the mother liquor obtained on recrystallizing the dihydroxyethylglycine monobenzoate a gelatinous mass remains which, unlike the original crystalline product, is soluble in benzene and similar solvents and forms a picrate which does not differ from the picrate of hydroxyet hylmorpholone benzoate. No matter how pure is the open ester taken for crystallization, the mother liquor will always contain the lactone. In this case also, therefore, an equilibrium is established between the hydroxy acid and its lactone.

An attempt was made to synthesize the monobenzoate of dihydroxyethylglycine directly from the dihydroxy acid. The reaction was carried out between benzoyl chloride and dihydroxyethylglycine in a pyridine medium, using a molar ratio of 1:1. In place, however, of the monoester of the dihydroxy acid which should have been obtained in the normal course of the reaction, the original dihydroxyethylglycine was recovered from the reaction mixture (nearly 40% of the original amount was recovered), and benzoic acid and hydroxyethylmorpholone benzoate were also formed.

A similar attempt to synthesize the dibenzoate from dihydroxyethylglycine and two molecules of benzoyl chloride (in pyridine) was also unsuccessful. In this case again, instead of the anticipated dibenzoyl derivative, the benzoate of hydroxyethylmorpholone was obtained. Such a course of the benzoylation of dihydroxyethylglycine becomes intelligible if we assume the following mechanism. The first step is the normal process of esterification to form the monobenzoate of dihydroxyethylglycine(V). We have shown, however, that the monobenzoate of dihydroxyethylglycine in solution (especially when hot) is in equilibrium with the benzoate of hydroxyethylmorpholone (II). Since the benzoyl chloride-pyridine complex is know to avidly absorb water, the latter is progressively removed from the sphere of reaction. The equilibrium is consequently shifted to the right, i.e., in the direction of formation of the morpholone derivative, as we also observed in our experiments. Hence the sole route to preparation of the monoesters of dihydroxyethylglycine lies through the step of isolation of the esters of hydroxyethylmorpholones followed by their hydrolysis.

The dibenzoate of dihydroxyethylglycine could only be prepared by benzoylation in an alkaline medium (Schotten-Baumann). It proved to be not identical in properties with the compound synthesized by an analogous method by Kiprianov [2] this compound according to Kiprianov, was a soft, easily fusible mass which formed a benzoylethyl ester when recrystallized from alcohol. The dibenzoyl derivative of dihydroxyethylglycine that we prepared had a well-defined crystalline structure, melted sharply at 142° and did not undergo any decomposition when recrystallized from methanol or ethanol. Its structure as the dibenzoate of dihydroxyethylglycine (VII) was confirmed by the elementary



(VII)

analysis and by all its properties. As shown by our observations the tendency of monoesters of dihydroxyethylglycine to change into the lactone is in definite relation to the degree of basicity of the formed morpholone derivatives. The weaker the basic properties of the cyclic product the more easily is it formed and the more stable it is. Such a relation between the stability of morpholone derivatives and their basicity is conspicuous when we compare the properties of hydroxyethylmorpholone and its esters.

The basic properties of hydroxyethylmorpholone are fairly well marked. Its aqueous solutions have a weakly alkaline reaction to brilliant yellow paper (pH about 7.5), the hydrochloride is quite stable in the crystalline form and does not undergo appreciable dissociation on prolonged heating at temperatures not higher than its melting point (139°).

By contrast hydroxyethylmorpholone has poor stability in the form of its free base, after only a few days in the air it is covered with a dense crust of dihydroxyethylglycine due to hydrolysis. The basic properties and stability of esters of hydroxyethylmorpholone are in marked contrast. All of the three esters which we have studied (acetate, benzoate and diphenylacetate) possess negligible basicity. Their aqueous solutions (admittedly very dilute) have a neutral reaction to all the usual indicators with a color change in the pH range of 5 to 7 (e.g. methyl red and litmus). Attention has been drawn above to the instability of their hydrochlorides. Note has also been made of the extra ordinarily low basicity of the diphenylacetate which does not even form a picrate. On the other hand, the esters

of hydroxyethylmorpholone are much more stable than the original amino alcohol and can be exposed to the air without appreciable hydrolysis over a period of days. The diphenylacetate is particularly stable, which is fully consistent with its very low basicity. The same considerations may be said to apply to the ease of closure of the morpholone ring. Here a convenient criterion is the melting point of dihydroxyethylglycine and its monoesters, since this temperature is essentially not only the point of change of physical state but is also to a great extent the point of transformation of the hydroxy acid into its lactone (accompanied by closure of the morpholone ring). The lower the melting point of the compound in question, the more easily (in otherwise identical conditions) is the morpholone derivative formed.

In the table below are listed the "melting" points of dihdroxyethylglycine and of its three monoesters.

Substance	Temperature of transformation* into lactone
Dihydroxyethylglycine	190-192°
" monoacetate	102-104
" monobenzoate	127-127.5
" diphenylacetate	82-84

The data in the table show that dihydroxyethylglycine changes into the morpholone derivative much less readily than its monoesters. Of the latter the diphenylacetate forms the lactone with the greatest ease. The basic properties of the diphenylacetate, as repeatedly observed, are the weakest of all the esters. Such a correlation between the basicity of the morpholones and their stability is also in accord with the fact that N,N-arylhydroxyethylglycines generally cannot be obtained in the free state, because they are transformed into the corresponding N-arylmorpholones on simple acidification of solutions of their salts. Yet for the purpose of cyclization of the N,N-alkylhydroxyethlglycines it is necessary to have recourse to dry distillation in vacuum, the resultant alkylmorpholones being readily hydrolyzed with transformation into the original acids [3].

EXPERIMENTAL

Benzoate of N-hydroxyethylmorpholone. 3.36 g (0.023 mole) freshly distilled hydroxyethylmorpholone or 4.18 g of its hydrochloride was dissolved in twice the volume of dry pyridine, and to the cooled (ice water) pyridine solution was slowly added (with energetic shaking) from a dropping funnel benzoyl chloride in the amount of 3.3 g (0.0235 mole), and the residue in the funnel washed out with 0.5 ml dry benzene. The reaction flask was fitted with an air condenser and protected in the usual manner against access of atmospheric moisture. The mixture was heated on the water bath for 2-3 hours, after which it was cooled and the formed viscous crystalline mass was diluted with dry xylene. The xylene-pyridine solution was filtered from the precipitate of pyridine hydrochloride and evaporated to a very small volume in vacuum. The residue was diluted with dry xylene; the solution was filtered (if necessary) and again evaporated down in vacuum. The residue was dissolved in benzene, dried over BaO and after distillation of the benzene, distilled in vacuum. The yield of fraction with b.p. 210-212° at 3.5 mm was 4.0-4.2 g or 69-72% of the theoretical. This is a glycerol-like, colorless liquid soluble in aromatic hydrocarbons, ether and all polar solvents, but poorly soluble in water. When kept in an open vessel for several weeks it gradually hydrolyzes to form the monobenzoate of dihydroxyethylglycine.

0.1946 g substance: 0.4454 g CO_2, 0.1094 g H_2O. 0.1520 g substance: 0.3486 g CO_2, 0.0842 g H_2O. 0.3726 g substance: 18.0 ml N_2 (24°, 766 mm). 0.3212 g substance: 15.7 ml N_2 (24°, 763 mm).
Found %: C 62.46, 62.58; H 6.30, 6.20; N 5.59, 5.64. $C_{13}H_{15}O_4N$. Calculated %: C 62.66; H 6.07; N 5.62.

Picrate of the benzoate of N-hydroxyethylmorpholone. Prepared by mixing equimolar amounts of hot benzene solutions of the ester and picric acid. The picrate forms bright-yellow, elongated, acicular prisms (from glacial acetic acid + acetone). M.p. 204-206° (with decomposition). Soluble in water, acetone and glacial acetic acid, poorly soluble in methanol and ethanol. Insoluble in nonpolar solvents.

0.1054 g substance: 0.1842 g CO_2, 0.0360 g H_2O. 0.1104 g substance: 0.1918 g CO_2, 0.0352 g H_2O.
0.1390 g substance: 14.6 ml N_2 (24°, 743 mm). 0.1434 g substance: 16.0 ml N_2 (25°, 738 mm).
Found %: C 47.69, 47.41; H 3.82, 3.57; N 11.81, 11.92. $C_{19}H_{18}O_{11}N_4$. Calculated %: C 47.70; H 3.79; N 11.71.

Monobenzoate of dihydroxyethylglycine. 2.5 g distilled hydroxyethylmorpholone benzoate was mixed with 5 ml water and heated on the water bath until the boundary between the layers of oil and water had disappeared. The residue

* Here, as elsewhere in the text, the temperatures have been corrected for the exposed stem of the thermometer.

was diluted with water (this caused the oil to separate again) and again evaporated on the water bath until a thick, gelatinous mass had formed; this was cooled (ice bath) and seeded; after a few hours it crystallized. The so-obtained solid product was pulverized, treated with acetone and pressed on the filter. Yield 1.85-2.0 g or 80-85% of the theoretical. After recrystallization from methanol or ethanol (preferably with acetone) the substance melted at 127-127.5° (on heating the capillary, starting at 120°) and formed colorless needles (under the microscope). It is highly soluble in water, hot methanol, ethanol and glacial acetic acid; moderately soluble in cold methanol and ethanol; still less soluble in acetone. Its solubility in nonpolar solvents is negligible. No matter how pure was the initial monobenzoate of the dihydroxy acid, the alcoholic mother liquors, after their crystallization, always contained the benzoate of hydroxyethylmorpholone, since, after evaporation of the alcohol (in the air), an oil remained which gave a picrate with an m.p. 200-204°, identical with hydroxyethylmorpholone benzoate picrate (mixed m.p. 202-205°).

0.0782 g substance: 0.1680 g CO_2; 0.0448 g H_2O. 0.1444 g substance: 0.3085 g CO_2; 0.0854 g H_2O. 0.1692 g substance: 8.0 ml N_2 (24°, 750 mm). 0.2710 g substance: 12.6 ml N_2 (23°, 761 mm). Found %: C 58.63, 58.30; H 6.41, 6.62; N 5.36, 5.37. $C_{11}H_{13}O_3N$. Calculated %: C 58.41; H 6.41; N 5.24.

Attempt to prepare the monobenzoate of dihydroxyethylglycine from dihydroxyethylglycine and benzoyl chloride. To 1.63 g (0.01 mole) dihydroxyethylglycine in 10 ml dry pyridine was added dropwise 1.41 g (0.01 mole) benzoyl chloride. The amount of solid dihydroxyethylglycine appreciably lessened. The mixture was heated on the water bath (in a flask fitted with an air condenser and a calcium chloride tube) for 3 hours, after which it was cooled and the pyridine solution was poured off from the insoluble pasty, resinous, colorless mass which remained at the bottom of the reaction flask. The pyridine solution was diluted with twice the volume of dry xylene, filtered from the precipitate of pyridine hydrochloride and evaporated down in vacuum. The residue after evaporation was diluted with xylene and again evaporated. The resultant thick, crystalline slurry was carefully treated with cold benzene and the benzene extract was mixed with a benzene solution of picric acid. A precipitate of the picrate of hydroxyethylmorpholone with m.p. 203-[illegible]° was obtained (mixed m.p. 204-206°). The benzene-insoluble crystalline precipitate of benzoic acid was recrystallized from aqueous alcohol. M.p. 120°. A mixed sample with benzoic acid melted at 120-121°. The resinous material remaining in the flask was treated with absolute alcohol to give a white crystalline precipitate with m.p. 175-178°, weight 0.64 g. After recrystallization from 80% methanol it melted at 186-189°. A mixture with dihydroxyethylglycine melted at 184-190°. Consequently, the treatment of dihydroxyethylglycine with an equimolar amount of benzoyl chloride resulted in formation of the benzoate of hydroxyethylmorpholone. Half of the original benzoyl chloride was separated by addition of water and was converted into benzoic acid. Correspondingly, one half of the original dihydroxyethylglycine remained unchanged.

Attempt to prepare the dibenzoate of dihydroxyethylglycine from dihydroxyethylglycine and benzoyl chloride. The reaction was performed as described above except that the molar ratio of dihydroxy acid and benzoyl chloride was 2:1. The actual quantities were 0.82 g (0.005 mole) dihydroxy acid and 1.42 g (0.01 mole) benzoyl chloride. Reaction products were hydroxyethylmorpholone benzoate (identified as the picrate) and benzoic acid. The original dihydroxyethylglycine could not be detected in the reaction mixture.

Dihydroxyethylglycine dibenzoate. To a solution of 1.63 g (0.01 mole) dihydroxyethylglycine in 5 ml water was added (with energetic shaking in a flask with a ground-glass stopper) alternately a 25% NaOH solution and benzoyl chloride in such a manner that the medium always remained alkaline to phenolphthalein and not too much unreacted benzoyl chloride accumulated. From time to time the reaction mixture was cooled to room temperature. In this manner a total of 13.0 ml 25% NaOH (0.081 mole) and 6.05 g (0.043 mole) benzoyl chloride was added. After the whole of the benzoyl chloride had entered into reaction (indicated by the disappearance of the oily drops), the perfectly homogeneous solution was carefully acidified with 10 N hydrochloric acid until weakly acid to litmus but not yet acid to Congo. The snow-white precipitate was filtered, well pressed on the filter and transferred to a beaker where it was triturated with 1-2 ml ethanol and 8-10 ml ether for purification from benzoic acid. The suspension was filtered, and the precipitate washed with ether. Yield 1.30-1.36 g or 70-73% of the theoretical. The substance crystallizes from methanol or ethanol in the form of long, soft needles resembling asbestos fiber; m.p. 141.5-142.5°. Readily soluble in acetone, benzene, chloroform, hot methanol and ethanol; less soluble in cold water and ether.

0.1268 g substance: 0.3006 g CO_2; 0.0680 g H_2O. 0.2032 g substance: 0.4796 g CO_2; 0.1068 g H_2O. 0.3120 g substance: 10.5 ml N_2 (22°, 740 mm). 0.6510 g substance: 21.5 ml N_2 (24°, 750 mm). Found %: C 64.69, 64.41; H 6.00, 5.88; N 3.79, 3.75. $C_{18}H_{17}O_4N$. Calculated %: C 64.67; H 5.70; N 3.77.

N-Hydroxyethylmorpholone acetate. 4.35 g (0.03 mole) hydroxyethylmorpholone or the equivalent amount of its hydrochloride, was dissolved in 2-3 times the volume of dry pyridine, and into the obtained solution was gradually run,

while cooling and excluding atmospheric moisture (the reaction was carried out in a flask fitted with a dropping funnel and an air condenser with a calcium chloride tube), 1.5 g (0.019 mole) acetyl chloride. The mixture was then left at room temperature for 30-40 minutes and the reaction completed by heating for an hour on the water bath. The so-obtained dark-red (sometimes brownish-yellow) pyridine solution was cooled and formed a crystalline slurry which was diluted with twice the volume of dry xylene; the crystals of pyridine hydrochloride were separated by filtration. The filtrate was freed from pyridine by evaporation in vacuum; the residue from the evaporation was diluted with xylene and the precipitate was filtered off. The xylene was then distilled off in vacuum and the residue distilled at 5 mm to give a fraction at 165-171°. Yield 2.0-2.1 g or 63% of the theoretical. Properties: colorless liquid, boiling at 167-168° (5 mm residual pressure), readily soluble in water and all other common solvents except gasoline, carbon tetrachloride and ether.

0.1816 g substance: 0.3428 g CO_2; 0.1163 g H_2O. 0.1488 g substance: 0.2804 g CO_2; 0.0944 g H_2O. 0.2954 g substance: 18.8 ml N_2 (23°, 772 mm). 0.3258 g substance: 21.1 ml N_2 (24°, 775 mm).

Found %: C 51.51, 51.42; H 7.17, 7.10; N 7.46, 7.59. $C_8H_{15}O_4N$. Calculated %: C 51.33; H 7.00; N 7.48.

N-Hydroxyethylmorpholone acetate picrate. Prepared by mixing an alcoholic solution of the base with a hot concentrated benzene solution of the equivalent amount of picric acid. The oil formed crystallized rapidly. Yellow prisms (from acetone-methanol), sparingly soluble in common solvents excepting glacial acetic acid and acetone. M.p. 167-168°.

0.1778 g substance 0.2639 g CO_2 0.0624 g H_2O. 0.2212 g substance: 0.3298 g CO_2; 0.0788 g H_2O. 0.1266 g substance: 15.2 ml N_2 (24°, 755 mm). 0.1607 g substance: 19.4 ml N_2 (24°, 750 mm).

Found %: C 40.50, 40.69; H 3.93, 3.99; N 13.71, 13.69; $C_{14}H_{16}O_{11}N_4$. Calculated %: C 40.39; H 3.88; N 13.46.

Picrolonate of N-hydroxyethylmorpholone acetate. Prepared by mixing hot concentrated solutions in absolute alcohol of hydroxyethylmorpholone acetate and picrolonic acid (equimolecular amounts). The substance forms long yellow prisms (from glacial acetic acid), m.p. (with decomp.) 186-187.5°. Solubility like that of the picrate.

0.1556 g substance: 0.2751 g CO_2; 0.0666 g H_2O. 0.1500 g substance: 0.2645 g CO_2; 0.0637 g H_2O. 0.0934 g substance: 12.8 ml N_2 (24°, 760 mm). 0.1547 g substance: 20.7 ml N_2 (24°, 773 mm). Found %: C 48.29, 48.13; H 4.79, 4.75; N 15.75, 15.64. $C_{18}H_{21}O_9N$. Calculated %: C 47.89; H 4.69; N 15.53.

Monoacetate of N,N-dihydroxyethylglycine. 2 g N-hydroxyethylmorpholone acetate was dissolved in 10-15 ml water and the solution was evaporated on the water bath to a thick, yellowish syrup. Evaporation was then continued in vacuum (at the temperature of the boiling water bath) and the resultant resinous mass was kept in a vacuum desiccator over KOH until it solidified.

The solid, amorphous product was reduced to powder, treated with 4-5 ml boiling acetone, filtered from mother liquor, dried and recrystallized from methanol-acetone. M.p. 102.5-104°. Very soluble in water, lower alcohols and glacial acetic acid; poorly soluble in acetone and ether.

0.1550 g substance 0.2660 g CO_2; 0.1030 g H_2O. 0.1740 g substance: 0.2986 g CO_2; 0.1140 g H_2O. 0.2630 g substance: 16.3 ml N_2 (24°, 754 mm). 0.2248 g substance: 13.5 ml N_2 (24°, 760 mm). Found %: C 46.83, 46.83; H 7.44, 7.46; N 7.07, 6.90. $C_8H_{15}O_5N$. Calculated %: C 46.82, H 7.37; N 6.83.

Partial diphenyl acetate of dihyroxyethylglycine. 1.9 g freshly distilled hydroxyethylmorpholone (0.0105 mole) was placed in a small flask fitted with an air condenser and a calcium chloride tube. 7 ml dry pyridine was added to the flask, into the resultant solution was introduced in small portions with vigorous shaking, crystalline diphenylacetyl chloride in quantity of 2.42 g (0.0105 mole). The last portions of acid chloride dissolved with much difficulty in the reaction mixture and gentle heating was then necessary. After the whole of the acid chloride had been added, the mixture was heated on the boiling water bath for 3 hours, then cooled, diluted with 12-15 ml dry xylene, and the precipitated pyridine hydrochloride filtered off. The filtrate was evaporated in vacuum (to get rid of pyridine) and the residue was again diluted with 7-10 ml dry xylene. The xylene solution was separated from the small precipitate, stood overnight with BaO (for decolorization) and then filtered. The solvent was distilled off in vacuum. The residual diphenylacetate of hydroxyethylmorpholone was a thick, oily liquid with a brownish-orange color. It could not be purified by distillation since it did not distill at 3 mm residual pressure.

For conversion into the diphenylacetate of dihydroxyethylglycine the unpurified diphenylacetate of hydroxyethylmorpholone was mixed with 5-6 ml water, and the unstable emulsion was heated on the water bath for 5 hours,

the volume of heated liquid being kept constant by addition of water to make up for the loss by evaporation. The liquid was later cooled to room temperature and after addition of a seed of crystalline diphenylacetate of dihydroxyethylglycine it was left for a few hours to crystallize. The resultant crystal slurry was diluted with a very small amount of water and transferred to a filter on which it was expressed under vacuum, twice washed with a little ice water and again pressed. The moist cake was dried on filter paper and then transferred to a vacuum desiccator containing calcium chloride in which it was brought to the air-dry state. Yield 3.16 g or 86% of the theoretical. After recrystallization from chloroform-ether the substance melted at 82-84° • and was in the form of long, soft needles (under the microscope), easily soluble in the majority of organic solvents, poorly soluble in water, ether and gasoline.

0.1290 g substance: 0.3174 g CO_2; 0.0768 g H_2O. 0.1105 g substance: 0.2721 g CO_2, 0.0646 g H_2O. 0.4118 g substance: 13.4 ml N_2 (21°, 744 mm). 0.5112 g substance: 16.6 ml N_2 (21°, 739 mm). Found %: C 67.14, 67.20; H 6.66, 6.54; N 3.70, 3.67. $C_{20}H_{23}O_5N$. Calculated %: C 67.21; H 6.49, N 3.92.

N-Hydroxyethylmorpholone diphenylacetate. As stated above, the diphenylacetate of hydroxyethylmorpholone synthesized from hydroxyethylmorpholone and diphenylacetyl chloride could not be purified by distillation. The pure compound was therefore prepared by dehydration of dihydroxyethylglycine diphenylacetate, the reaction proceeding quantitatively and in mild conditions. The weighed amount of the initial ester of dihydroxyethylglycine was placed in a thick-walled test tube which was then connected to a vacuum through a rubber stopper and a leading tube. It was heated at a residual pressure of 10-15 mm on a water bath kept at a temperature of 85-95°. Heating was continued until the test tube and contents had a constant weight: this required 1½ - 2 hours. The diphenylacetate of hydroxyethylglycine was obtained in quantitative yield in the form of a transparent, very viscous liquid with a tinge of yellow, soluble in all the common organic solvents (except saturated hydrocarbons) and sparingly soluble in water. The aqueous solution was neutral to litmus.

0.5141, 0.6755 g dihydroxyethylglycine diphenylacetate: loss in weight after heating in vacuum 0.0251, 0.0338 g. Found loss in weight %: 4.88, 5.00. Calculated loss in weight %: 5.04. Reaction equation $C_{20}H_{23}O_5N - H_2O = C_{20}H_{21}O_4N$.

Picrolonate of N-hydroxyethylmorpholone diphenylacetate. Prepared by mixing a benzene solution of the diphenylacetate with a solution of picrolonic acid in absolute alcohol. The oil that separated gradually crystallized. The picrolonate forms a yellow crystalline powder with m.p. 135-138°. Soluble in methanol and ethanol. On cooling the alcoholic solutions, it separated as an oil which resisted all attempts at crystallization. It was not subjected to elementary analysis because it could not be obtained pure.

SUMMARY

1. For the first time the acetate, benzoate and diphenylacetate of N-(β-hydroxyethyl)-morpholone-2, their picrates and picrolonates have been synthesized and their properties have been studied.

2. For the first time, by hydrolysis of esters of hydroxyethylmorpholone, the corresponding monoesters of dihydroxyethylglycine have been prepared, these could not be obtained directly from dihydroxyethylglycine and the acid chlorides.

3. On the basis of a comparison of the properties of hydroxyethylmorpholone and its esters it is suggested that a reciprocal relation exists between the stability and the basicity of morpholone derivatives. The greater the basicity of a morpholone derivative the more easily does opening of the morpholone ring take place and the less easily is it formed.

4. The dibenzoate of dihydroxyethylglycine has been synthesized for the first time.

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• It melts slowly and therefore does not possess a sharp melting point.

•• See Consultants Bureau English translation, page 621.

SYNTHESIS AND TRANSFORMATIONS OF SOME DERIVATIVES OF N,N-DI-(β-HYDROXYETHYL)-GLYCINE

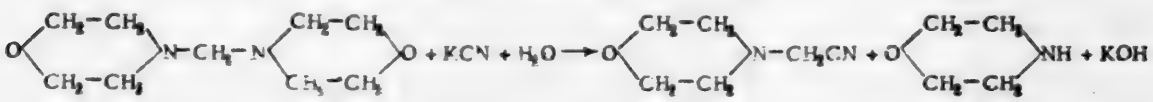
III. SYNTHESIS OF 4-MORPHOLINEACETIC ACID

A. L. Remizov and N. V. Khromov

In our preceding communication [1], it was indicated that the hydrochloride of N,N-di-(β-hydroxyethyl)-glycine undergoes dehydration when heated in vacuum, and that this reaction would be expected to yield two isomeric compounds (in the form of hydrochlorides): N-hydroxyethylmorpholone-2 and 4-morpholine-acetic acid.

Since the hydrochlorides of these two compounds have not been described in the literature and attempts to prepare the salt of the first compound from the free base were unsuccessful, it was proposed to synthesize morpholine-4-acetic acid with the aim of establishing the structure of our product of dehydration of the hydrochloride of dihydroxyethylglycine.

Although neither free morpholineacetic acid nor its hydrochloride, have been described in the literature, a series of other derivatives (including the potassium salt) was already known [2]. The described method of preparation of these compounds is not simple. It is based on the reaction between 4,4'-dimorpholylmethane (product of condensation of morpholine with formaldehyde) and KCN. This reaction gives one molecule of 4-morpholine-acetonitrile and one molecule of morpholine:



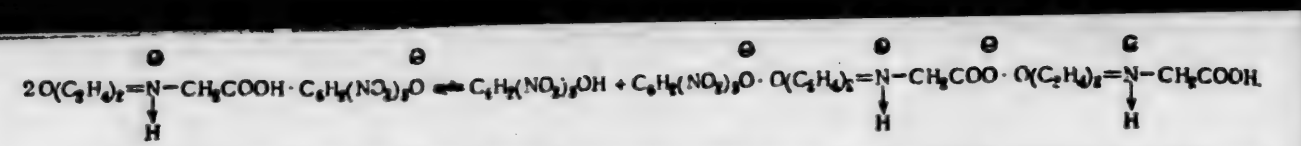
Our own synthesis of 4-morpholine-acetic acid consisted in condensation of morpholine with monochloroacetic acid (as sodium salt) according to the usual reaction.

Morpholine was obtained by dehydrating diethanolamine in concentrated sulfuric acid as described by Medard [3].

The synthesized morpholineacetic acid proved to be so hygroscopic and uncrystallizable that it was impossible to obtain pure. It was transformed into the barium salt and the hydrochloride. Of these salts, only the second possessed adequate stability and crystallizing ability. It was analyzed.

An interesting characteristic of morpholineacetic acid is its ability to form two picrates: one of these is formed from equimolar amounts of components and the other from 1 mole picric acid and two moles morpholineacetic acid. The second picrate (we may call it "semipicrate") is very much more stable than the first, which is appreciably dissociated in solution to form the "semipicrate" and free picric acid. This mode of dissociation is particularly conspicuous when the normal picrate is dissolved in alcohol: the "semipicrate" is very sparingly soluble in alcohol and comes down from alcoholic solutions of the normal picrate in the form of a precipitate. This dissociation of morpholineacetic acid picrate is reversible and only proceeds up to a certain limit. Hence, the precipitated "semipicrate" can again be transformed into normal picrate by adding a small amount of excess picric acid. This explains why the normal picrate can be prepared in the pure form only by recrystallization in presence of a small amount of excess picric acid.

If we assume that the normal picrate of morpholineacetic acid also functions as a base, then the "semipicrate" may be regarded as a salt of the normal picrate (functioning as an acid) with morpholineacetic acid (functioning as a base). The superior stability of the "semipicrate" and the very fact of its formation indicate that the free carboxyl group of the normal picrate possesses more pronounced acidic properties than the carboxyl group of morpholineacetic acid. Considering the problem from this standpoint, we may reach the conclusion that the normal picrate approaches picric acid in its acidic properties. Actually, on reacting two molecules of the normal picrate, one of them (playing the part of acid) displaces picric acid from the other (acting as salt). In this way we can account for the ability of morpholineacetic acid picrate to dissociate in solutions, as expressed by the scheme



In the course of investigation of the properties of morpholineacetic acid, the dissociation constants were determined by potentiometric titration of its hydrochloride. The apparent acidic ionization constant at 19° was equal to $10^{-7.7}$, the basic constant was $10^{-11.7}$; the corresponding Bjerrum values are $10^{-2.4}$ and $10^{-6.4}$.

EXPERIMENTAL

Barium salt of 4-morpholine-acetic acid. 8.5 g (0.09 g-mole) monochloroacetic acid was dissolved in 10 ml water and carefully neutralized (with cooling) with a solution of 3.6 g (0.09 g-mole) NaOH in 10 ml water. To the solution of sodium monochloroacetate (weakly alkaline to litmus and nearly neutral to Brilliant Yellow paper) was added dropwise, with moderate cooling, 7.85 g (0.09 g-mole) morpholine, after which the reaction mixture was stood at room temperature for 20 minutes and finally heated to the boil to complete the reaction. After boiling for 20 minutes, the medium had acquired a neutral reaction (prior to this it was strongly alkaline to Brilliant Yellow paper). The faint-yellow solution was evaporated on the water bath to a very thick syrup (further evaporation had no effect on the consistency) which was then treated with 75 ml absolute alcohol. The precipitated sodium chloride was filtered off, the filtrate was evaporated in vacuum and the residual gelatinous mass was mixed with a hot solution of 25 g barium hydrate in 70 ml water. The water was distilled off in vacuum, the distillate being collected in a receiver immersed in a freezing mixture. To the dry residue in the distillation flask was added another 80 ml water and the distillation repeated. The same operation was repeated once more. In all, three distillates were collected. They all had an alkaline reaction since they contained the morpholine which had been present in the reaction mass in the form of its salt with glycolic acid formed by the secondary reaction of hydrolysis of monochloroacetic acid. The morpholine content of the three alkaline distillates was determined by titration with acid.

The first distillate required 1.7 ml 2 N HCl or 0.0034 g-mole; the second required 22.0 ml 0.1 N HCl or 0.0022 g-mole, the third required 5.2 ml 0.1 N HCl or 0.0005 g-mole. Total 0.006 g-mole, corresponding to 6.7% or 0.09 g-mole of the original morpholine. Consequently the reaction had proceeded in the desired direction to the extent of 93%.

The white crystalline mass remaining after distillation of the water and the morpholine was stirred with 150 ml hot water and the excess barium hydrate was precipitated by a current of carbon dioxide (until disappearance of the alkaline reaction to thiazole blue paper). The solution of barium salt of morpholineacetic acid was filtered off from the barium carbonate and evaporated to dryness; the dry residue was treated with a small quantity of boiling absolute alcohol. After filtration from the alcoholic mother liquor the precipitate was washed on the filter with a little absolute alcohol, then with ether, and dried in a vacuum-desiccator over caustic alkali. Yield 19.1 g. The barium salt was a snow-white crystalline powder, very soluble in water (the aqueous solutions were alkaline to phenolphthalein), methanol and glacial acetic acid, sparingly soluble in ethanol (especially absolute) and almost insoluble in other organic solvents. In the air it rapidly took up carbon dioxide and increased in weight. It could not be purified by crystallization.

4-Morpholine-acetic acid. 14.95 g unpurified barium salt of morpholineacetic acid was dissolved in 50 ml water and the barium quantitatively precipitated as $BaSO_4$ with 2N sulfuric acid (test on filter paper with sodium rhodizonate). The solution was separated from the precipitate by centrifuging and evaporated to dryness first on the water bath and finally in a vacuum-desiccator over sulfuric acid. The slightly moist crystal mass was twice treated with dry acetone and then several times with absolute ether (for removal of glycolic acid). This treatment converted it into a dry crystalline powder. The crystalline morpholineacetic acid prepared in this manner proved to be exceptionally hygroscopic. It was very soluble in methanol, ethanol and glacial acetic acid, much less soluble in acetone, and quite insoluble in ether. It was impossible to purify it and determine its melting point. Yield 8.0 g.

4-Morpholine-acetic acid hydrochloride. 4.0 g crystalline morpholineacetic acid was mixed with 4 ml chemically pure hydrochloric acid (s.g. 1.19) and the mixture evaporated to dryness on the water bath; the resultant crystalline powder was dried in a vacuum-desiccator over solid KOH. Yield quantitative.

After recrystallization from a mixture of absolute alcohol and dry benzene, the compound melted at 169-171° (with frothing), good solubility in methanol, ethanol and glacial acetic acid, poor in acetone, ether and hydrocarbons. Under the microscope it had the form of regular rectangular plates.

0.2429 g substance: 14.7 ml N_2 (27°, 753 mm). 0.2586 g substance: 17.2 ml N_2 (20°, 753 mm). 0.3030 g substance: 0.2380 g AgCl. 0.2210 g substance: 0.1730 g AgCl. Found %: N 7.75, 7.68; Cl 19.48, 19.36. $C_6H_{12}O_3NCl$. Calculated %: N 7.71; Cl 19.53.

4-Morpholine-acetic acid picrate of the composition $O(C_2H_4)_2NCH_2COOH \cdot C_6H_2(NO_2)_3OH$. 0.75 g (0.0052 g-mole) morpholineacetic acid was dissolved in 3 ml absolute alcohol. A solution of 1.17 g picric acid (0.0051 g-mole) in 3 ml benzene was prepared separately. The solutions were mixed. After a short period the crystalline picrate started to come down slowly. The precipitate was filtered, washed on the filter with benzene and ether. Yield 1.52 g or 80% of the theoretical. The substance was recrystallized from alcohol to which a little picric acid had been added. It formed bright-yellow, long hexagonal prisms (under the microscope), very soluble in methanol, ethanol and glacial acetic acid and not quite so soluble in water and acetone. M.p. 141-142°.

Without the addition of picric acid it is impossible to completely dissolve the compound in alcohol because it decomposes with cleavage of free picric acid and is transformed into the other picrate richer in morpholineacetic acid and difficultly soluble in alcohol. The excess picric acid present during the recrystallization of the picrate thus functions as an inhibitor of dissociation of that picrate.

0.2579 g substance: 0.3642 g CO_2; 0.0870 g H_2O. 0.2372 g substance: 0.3352 g CO_2; 0.0804 g H_2O. 0.1198 g substance: 16.2 ml N_2 (26°, 753 mm). 0.1279 g substance: 17.0 ml N_2 (26°, 756 mm). Found %: C 38.54, 38.56. H 3.77, 3.79, N 15.29, 15.19. $C_{12}H_{14}O_{10}N_4$. Calculated %: C 38.50; H 3.77; N 14.97.

4-Morpholine-acetic acid picrate of the composition $[O(C_2H_4)_2NCH_2COOH]_2 \cdot C_6H_2(NO_2)_3OH$. 0.75 g (0.0052 g-mole) morpholineacetic acid was dissolved in the minimum amount of a mixture (1:1) of acetone and glacial acetic acid. A solution of 0.58 g (0.00253 g-mole) picric acid in 3 ml benzene was separately prepared. The solutions were mixed hot. A copious crystalline precipitate came down on cooling and was filtered and washed with alcohol and ether. Yield 1.1 g or 83.5% of the theoretical. After treatment with alcohol followed by recrystallization from a mixture of glacial acetic acid and benzene or absolute alcohol, the compound melted at 170-171°. It formed a pale yellow crystalline powder (slender, long needles under the microscope), readily soluble in glacial acetic acid and sparingly soluble in alcohol.

0.1570 g substance: 0.2414 g CO_2; 0.0708 g H_2O. 0.2280 g substance: 0.3476 g CO_2; 0.1032 g H_2O. 0.1205 g substance: 14.35 ml N_2 (20°, 744 mm). 0.1268 g substance: 15.2 ml N_2 (21°, 739 mm). Found %: C 41.96, 41.61; H 5.05, 5.06, N 13.58, 13.53. $C_{18}H_{25}O_{13}N_5$. Calculated %: C 41.62; H 4.85; N 13.49.

Determination of the ionization constants of 4-morpholine-acetic acid. The acidic and basic constants were determined from the pH values at the half-equivalent points in titration of the hydrochloride of the acid with 0.1 N NaOH solution. The necessary potentiometric measurements were performed with the help of a lamp potentiometer (system GIPKh) with a glass electrode and a saturated calomel half-element as the standard potential electrode.

0.1815 g (0.001 g-mole) morpholineacetic acid was dissolved in 70 ml distilled water, into the solution was run 5.00 ml 0.1 N NaOH. In this way one-half of the hydrochloric acid entering into the composition of the hydrochloride of the amino acid was neutralized, which corresponded to the point of half-equivalence of the amino group. The pH of the solution at this stage was 2.4 at a temperature of 19°. Since the ionic product of water at this temperature is $10^{-14.1}$, then the apparent basic ionization constant of 4-morpholine-acetic acid is $10^{-11.7}$.

For the determination of the pH at the half-equivalent point in respect to the carboxyl group, addition was made to the test solution of a further 10.0 ml 0.1 N NaOH. This brought the pH to 7.7 and, consequently, the apparent acidic ionization constant of 4-morpholine-acetic acid is $10^{-7.7}$ at 19°.

On the basis of the data obtained by the above method the true ionization constants of morpholineacetic acid were calculated by the usual method (Bjerrum) and found to be $10^{-3.4}$ for the acid constant and $10^{-6.4}$ for the base constant.

SUMMARY

1. Free 4-morpholine acetic acid and its hydrochloride were synthesized and described for the first time.

2. The constants of electrolytic dissociation of 4-morpholine acetic acid were determined.

3. It was found that 4-morpholine-acetic acid forms two picrates with different picric acid contents (1 mole and ½ mole picric acid per mole of morpholineacetic acid).

*GIPKh = State Institute of Applied Chemistry. Publisher.

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* See Consultants Bureau English translation, page 621.

ORGANIC ISOCYANATES

II. TRANSFORMATION OF ISOCYANATES OF THE NAPHTHALENE SERIES BY THE ACTION OF ALUMINUM CHLORIDE

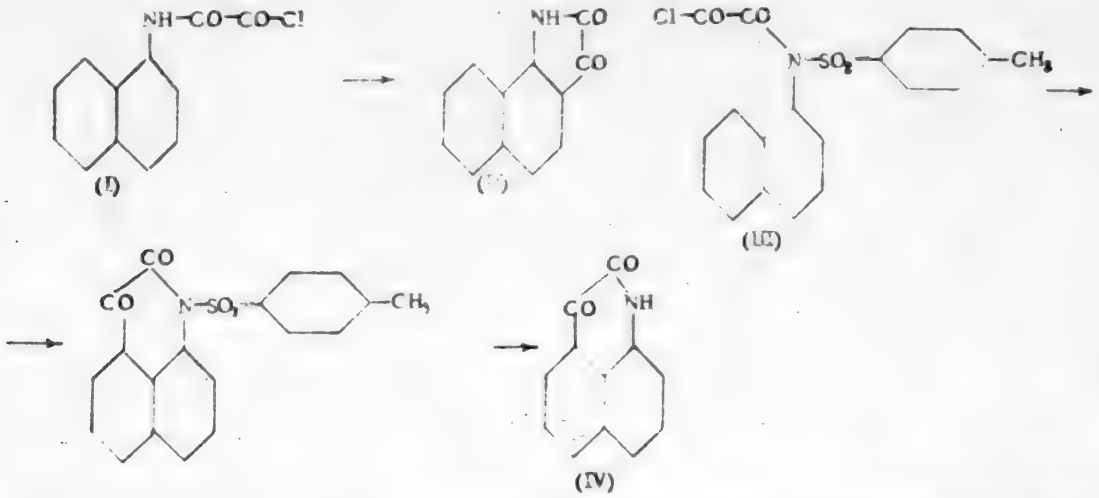
N. S. Dokunikhin and I. D. Pletneva

We previously reported [1] that 1-naphthylisocyanate is converted by fused aluminum chloride into the lactam of 1,8-aminonaphthoic acid (naphthostyril). In view of the fact that isocyanates of the benzene series in these conditions form derivatives of dioxotetrahydroquinazoline [2], from which salts of o-aminocarboxylic acids may be obtained by heating with caustic alkali, the entry of the isocyanate group into the 8-position of the naphthalene nucleus is unexpected. These facts make an investigation of the directive influence of the isocyanate group of interest. The latter group may be regarded as an amino group with both the hydrogen atoms substituted by acyl radicals. The literature does not throw any light upon the characteristics of the directive effects of either isocyanates or diacylamino derivatives.

In the majority of cases the introduction of a fresh substituent into diacyl derivatives obtained with participation of monocarboxylic acids gives rise to monoacyl derivatives. Thus, for instance, on nitration of diacetanilide the product is 4-nitro-1-acetanilide [3]. It is difficult to establish whether cleavage of the second acyl residue precedes the introduction of the fresh substituent or whether the monoacylated product is formed in consequence of decomposition of the substituted compound. In this connection more information can be obtained from data relating to cyclic aryl imides of dicarboxylic acids. This grouping remains unchanged during the majority of substitutions of the aromatic nucleus. Thus, for example, by nitration of diacylanilides we obtain p- and o-isomers, just as for monosubstituted derivatives [4]. Nitration of phthaloylnaphthylamines gives up to 60% 1,8-isomer, up to 28% 1,5-isomer and only 5% 1,4-isomer [5].

A similar orientation of substituents is observed with halo derivatives which combine o-, p-orientation with deactivation of the aromatic nucleus, which in the case of naphthalene results in substitution in the second ring.

It is interesting to follow the orienting influence of mono- and diacyl derivatives in two more examples. Fusion of aluminum chloride with 1-naphthyloxamyl chloride gives 1,2-naphthoisatin [7]; in these conditions the N-sulfamide derivative of the same acid chloride is converted into compound (IV) [8].



Formation of naphthostyrils was investigated with reference to 1-naphthylisocyanate, 4-chloro-1-naphthylisocyanate and 2-methyl-1-naphthylisocyanate.

EXPERIMENTAL

1-Naphthylisocyanate was prepared by the action of carbonyl chloride on a suspension of 1-naphthylamine hydrochloride in trichlorobenzene at 170-180°, b.p. 268-270° (269-270° [9]).

Naphthostyril. 3.20 g 1-naphthylisocyanate is introduced into a mixture, heated to 155-160°, of 25.8 g anhydrous aluminum chloride and 6.2 g sodium chloride and stirred for 5 minutes. The reaction mass is poured onto ice water and the precipitate filtered off. One half of the precipitate is heated 3 hours with 50 ml 40% KOH and again filtered. The precipitate is washed free from alkali. The filtrate and the wash liquors are acidified with hydrochloric acid and boiled. A yellow precipitate is formed. Weight 0.45 g, m.p. 176-179°. From ethyl alcohol it forms prisms with m.p 180.4-181.4°. A mixture with the naphthostyril prepared by alkali fusion of naphthalene-1,8-cyanosulfonate (m.p. 180.6-181.6°) had m.p. 180.4-181.5°.

The second half of the precipitate is repeatedly extracted with boiling 2% sodium carbonate solution. On cooling the soda extract, a yellow crystalline precipitate comes down. Weight 0.47 g, m.p. 177-178°, from ethyl alcohol: prisms with m.p. 180.3-181.3°. A mixture with the naphthostyril prepared by alkali fusion of naphthalene-1,8-cyanosulfonate (m.p. 180.6-181.6°) melts, 180.4-181.5°.

4-Chloro-1-acetylaminonaphthalene is prepared from 1-acetylaminonaphthalene with m.p. 158-159° [10]. The prepared 4-chloro-1-acetylaminonaphthalene has m.p. 186.5-187.0° after one crystallization from aqueous methanol, and 189.5-189.8° after three crystallizations.

4-Chloro-1-naphthylisocyanate. Into 125 ml toluene solution of carbonyl chloride at 0−5° is introduced 40 g 4-chloro-1-naphthylamine with m.p. 95-99°, prepared by saponification of 4-chloro-1-acetylaminonaphthalene with m.p 186.5-187.0°. The reaction mass is heated to 95°, stirred for 2 hours at this temperature and filtered. The toluene is distilled off from the filtrate and the residue distilled at 1.5 mm and 116.5-117°. Yield 18.78 g of compound, from carbon tetrachloride it forms colorless, lanceolate crystals with m.p. 44.4-45.0°.

The same compound is obtained: 1) by phosgenation of fused 4-chloro-1-acetyl-aminonaphthalene; 2) by phosgenation of a suspension of 4-chloro-1-acetylaminonaphthalene in trichlorobenzene.

Found %: N 6.83, 6.84; M (in benzene) 194.9, 198.3, 194.4. $C_{11}H_6ONCl$. Calculated %: N 6.88; M 203.5.

With methyl alcohol the prepared isocyanate forms a precipitate of methyl-1-naphthylcarbamate, m.p. (from carbon tetrachloride) 149.3-149.7°; colorless prisms. A mixture with the compound prepared from 4-chloro-1-naphthylamine and methyl chloroformate (m.p. 149.6-149.9°), melts at 149.6-149.8°.

Found %: Cl 14.98, 15.01. $C_{12}H_{10}O_2NCl$. Calculated %. Cl 15.05.

4-Chloronaphthostyril. Into a fused mixture of 24.20 g anhydrous aluminum hydrochloride and 5.80 g sodium chloride at 115° is introduced 2.95 g 4-chloro-1-naphthylisocyanate, after stirring for 15 minutes the mass is poured onto ice water and the precipitate is filtered. Sodium carbonate extraction gives 1.42 g substance. From glacial acetic acid it forms bright-yellow, lanceolate crystals with m.p 273.1-274.7° (about 267° [11], 270° [12]). A mixed test (1:1) with the 4-chloronaphthylstyril prepared by chlorination of naphthostyril [11, 13] with m.p 273.3-273.7° melts at 273-274.3°.

Found %. Cl 17.37. $C_{11}H_6ONCl$. Calculated %: Cl 17.43.

2-Methyl-1-naphthylisocyanate is prepared by phosgenation of 59.7 g of a suspension of 2-methyl-1-naphthylamine hydrochloride [14] in trichlorobenzene at 160-170°. The isocyanate comes over when the reaction mass is fractionated in vacuum at 14 mm and 161-162°. Weight of product 33.22 g. Rhombic plates (from carbon tetrachloride), m.p 28.7-29.3°.

Found %: N 7.56, 7.41; M (in benzene) 173, 175, 174. $C_{12}H_9ON$. Calculated %: N 7.65; M 183.

With methyl alcohol the compound forms a white precipitate of methyl 2-methyl-1-naphthylcarbamate; from methyl alcohol it crystallizes in prisms with m.p. 148.7-149.5°. The mixture with the substance prepared from 2-methyl-1-naphthylamine and methyl chloroformate, m.p. 147.5-148.2°, melts at 147.5-148.7°.

Found %: N 6.75, 6.73. $C_{13}H_{13}O_2N$. Calculated %: N 6.51.

2-Methylnaphthostyril. Into a fused mixture of 24.20 g anhydrous aluminum chloride and 5.80 g sodium chloride at 115° is introduced 2.98 g 2-methyl-1-naphthylisocyanate. The mixture is stirred 15 minutes and poured onto ice water. The precipitate is filtered, extracted with boiling 2% sodium carbonate. On cooling, the extract deposits yellow crystals. Weight 0.47 g. From ethyl alcohol it crystallizes as yellow prisms, m.p. 213.9-214.1°.

Found %: N 7.62, 7.61; M (in camphor) 215.7. $C_{13}H_9ON$. Calculated %: N 7.65; M 183.

SUMMARY

1. Reaction of 1-naphthylisocyanate and its derivatives with fused aluminum chloride is found to give 8-amino-1-naphthoic lactam (naphthostyril) and its derivatives. The reaction was followed with 1-naphthylisocyanate, 4-chloro-1-naphthylisocyanate and 2-methyl-1-naphthylisocyanate.

2. The hypothesis is advanced that the isocyanate and diacylamino groups may be classed with halogens in respect to their directing effect on introduction of a fresh substituent into the aromatic nucleus, since they combine para-, ortho- orientation with deactivation of the aromatic nucleus.

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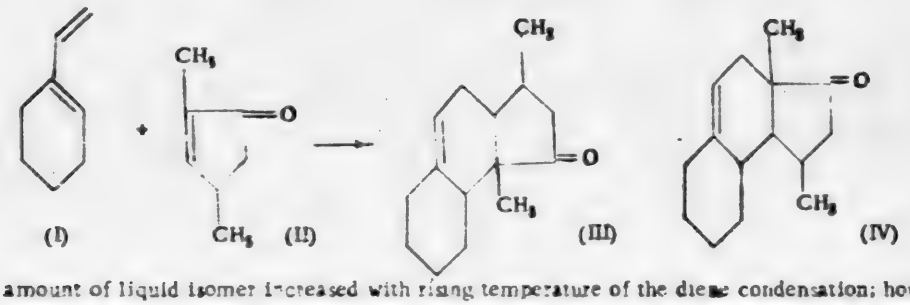
ACETYLENE DERIVATIVES. 154.

POLYCYCLIC HYDROCARBONS RELATED TO THE STEROIDS

XXVI. STRUCTURE OF THE TRICYCLIC KETONES PREPARED BY THE DIENE CONDENSATION OF 1-VINYL-Δ³-CYCLOHEXENE WITH 1,3-DIMETHYL-Δ⁴-CYCLOPENTEN-5-ONE

I. N. Nazarov and T. D. Nagibina

In one of the preceding investigations [1], it was shown that the diene condensation of 1-vinyl-Δ³-cyclohexene (I) with 1,3-dimethyl-Δ⁴-cyclopenten-5-one (II) gives two isomeric tricyclic ketones (a crystalline one with m.p. 61-62° and a liquid one with b.p. 147° at 7 mm), whose structure was represented by the formulas (III) and (IV):

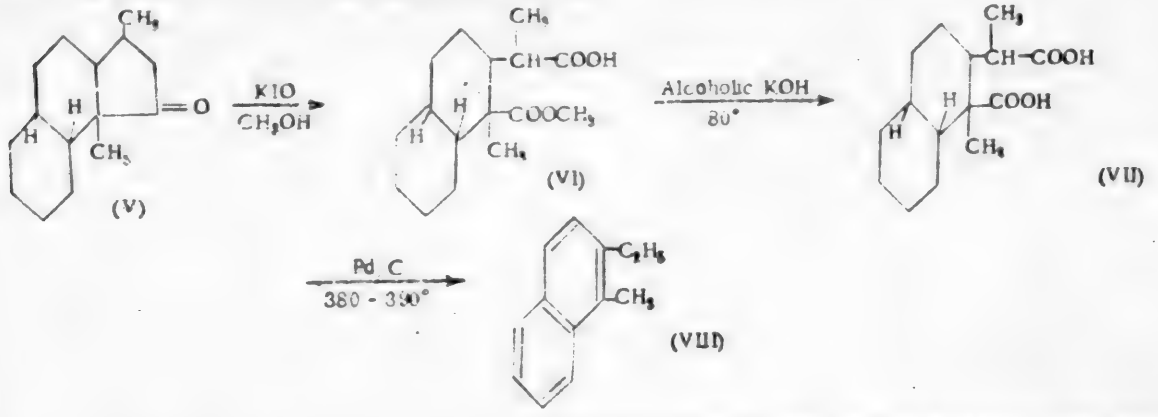


(I) (II) (III) (IV)

The amount of liquid isomer increased with rising temperature of the diene condensation; however, the crystalline isomer is not transformed into the liquid one even when heated in a glass ampoule at 200-210° for 20 hours.

In view of the fact that great interest attaches to the described diene condensation as the simplest model example for the synthesis of polycyclic compounds related to the steroids, we decided to undertake a direct demonstration of the structure of the tricyclic ketones that we obtained by this condensation. Another reason for doing this was the fact that little attention has hitherto been given to diene condensations of 1,2-substituted butadienes with asymmetrical dienophiles, although these condensations are of great theoretical and synthetic value.

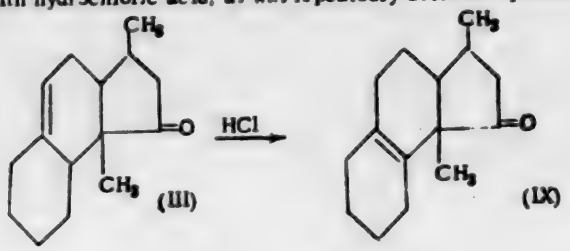
Detailed investigations revealed that the crystalline isomer with m.p. 61-62° was 1,9-dimethyl-4,5-tetramethylene-Δ⁵-hydrindane-3-one (III), whose structure was proved by hydrogenation to the saturated tricyclic ketone (V) and by oxidation of the ketone with iodine and alkali in methanol solution to the polyester of the dicarboxylic acid (VII); the latter was dehydrogenated and decarboxylated in presence of palladium-on-carbon at 380-390° to the known 1-methyl 2-ethylnaphthalene (VIII) [2].



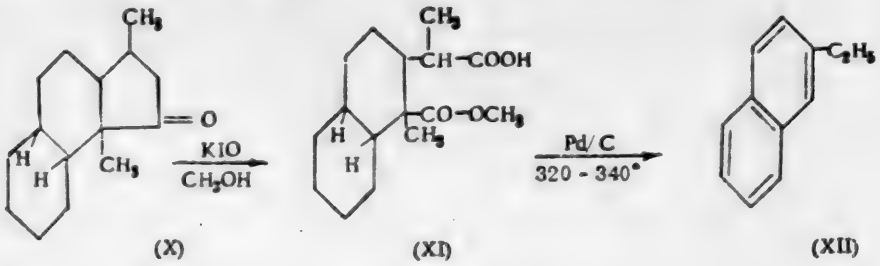
(V) (VI) (VII) (VIII)

A similar process of oxidative cleavage with the help of alcoholic iodine and alkali has recently been successfully employed to demonstrate the structure of some steroid ketones [3].

The liquid tricyclic ketone (b.p. 147° at 7 mm) proved to be 1,9-dimethyl-4,5-tetramethylene-Δ^4-hydrindane-3-one (IX), which was formed by diene condensation from the crystalline isomer (III) with double bond migration. This isomerization of the crystalline ketone (III) into the liquid isomer (IX) is realized with exceptional ease by heating with hydrochloric acid, as was repeatedly described previously in other cases [4]:



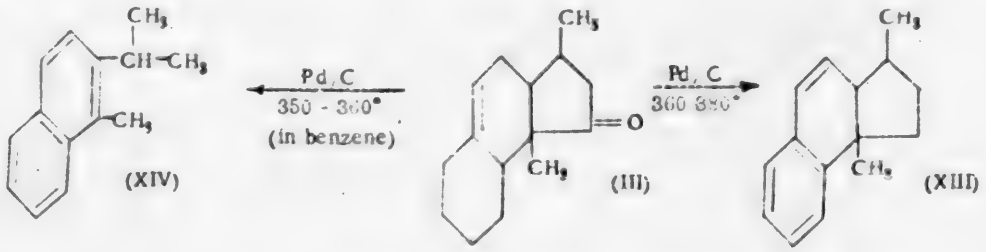
The structure of the liquid tricyclic ketone (IX) was also proved by hydrogenation to the saturated tricyclic ketone (X), oxidation of which with iodine and alkali in methanol solution gave the polyester (XI) which was dehydrogenated to 2-ethylnaphthalene (XII):



2-Ethylnaphthalene (XII) was also prepared by dehydrogenation of the above-described dicarboxylic acid (VII) with Ni catalyst (25 hours at 380-390°). It must be pointed out that hydrogenation with Pt catalyst of the tricyclic ketones (III) and (IX) leads to formation of different stereoisomeric ketones (V) and (X), differing in all probability by the configuration of the carbons at the place of addition of the first and second rings.

Consequently, in the diene condensation of 1-vinyl-Δ^3-cyclohexene (I) with 1,3-dimethyl-Δ^3-cyclopentene-5-one (II), only ketones (III) and (IX), which possess an identical skeleton and differ only in the position of the double bond, are formed. The ketone (IV), suggested above, is apparently not formed at all.

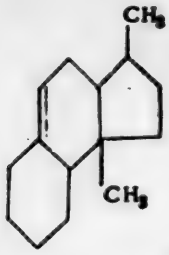
The tricyclic hydrocarbon (XIII) is formed on dehydrogenation of the crystalline ketone (III) with the help of palladium-on-carbon (5% Pd) at 360-380°. On carrying out this dehydrogenation in benzene solution, cleavage of the 5-membered ring occurs with formation of a hydrocarbon $C_{14}H_{16}$ which, in all probability, is 1-methyl-2-isopropylnaphthalene (XIV):

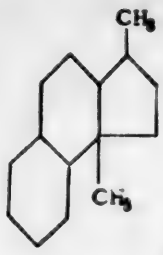


Such a dehydrogenation with cleavage of the five-membered ring has been successfully employed in recent years to establish the structure of steroid ketones [5].

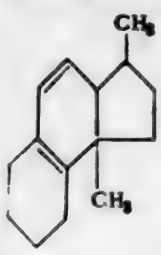
We also attempted to convert the tricyclic ketone (III) into 1-methyl-4,5-benzindane (XXIII), which we specially synthesized by two independent methods as described below. It was found, however, that the tricyclic ketone (III) is reduced by Kizhner's method with extraordinary difficulty to form the tricyclic hydrocarbon (XV) in small yield, while by Clemmensen's method, the ketone (III) is not reduced at all but only undergoes isomerization, with double-bond shift, to the liquid ketone (IX). In this connection it must be pointed out that Clemmensen's reduction fails to

occur with all other bi-, tri- and polycyclic ketones containing the 1,9-dimethyl hydrindane-3-one grouping [6]. The corresponding bi-, tri- and polycyclic hydrocarbons containing the 1,9-dimethylhydrindane grouping are extraordinarily resistant to exhaustive dehydrogenation with elimination of the angular methyl group [6]:


(XV)

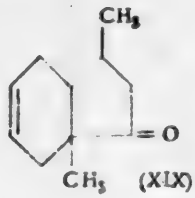

(XVI)

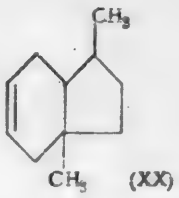
(XVII)

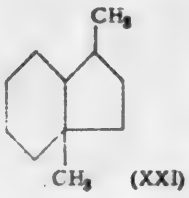

(XVIII)

By Kizhner's reduction of the saturated tricyclic ketone (V), it was possible to obtain in satisfactory yield (about 40%) the saturated tricyclic hydrocarbon (XVI) which, however, was not susceptible to exhaustive dehydrogenation to 1-methyl-4,5-benzindane (XXIII); even in very drastic conditions of dehydrogenation it only loses two molecules of hydrogen and is converted into a hydrocarbon with either structure (XVII) or (XVIII).

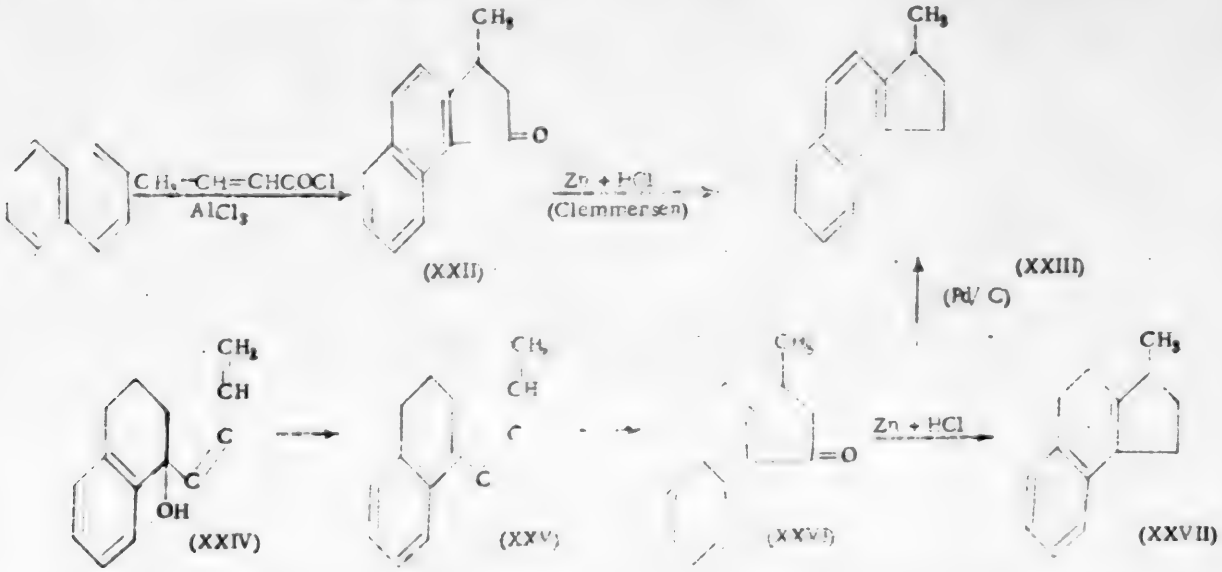
A similar striking stability in dehydrogenation conditions was also exhibited by the 1,9-dimethylhydrindanes (XX) and (XXI), prepared by Kizhner reduction of 1,9-dimethyl-Δ^{8}-hydrindane-3-one (XIX); this compound was synthesized in our laboratory previously by condensation of 1,3-dimethyl-Δ^{1}-cyclopentene-5-one (I) with butadiene [7]:


(XIX)

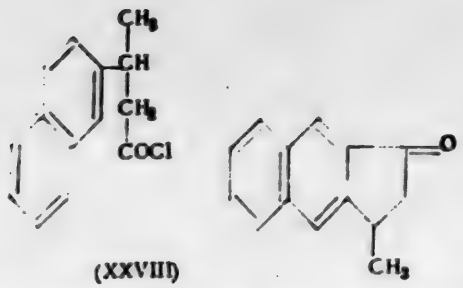

(XX)


(XXI)

1-Methyl-4,5-benzindane (XXIII), constituting the basis of the tricyclic ketones (III) and (IX), was synthesized by us by the two following independent routes:

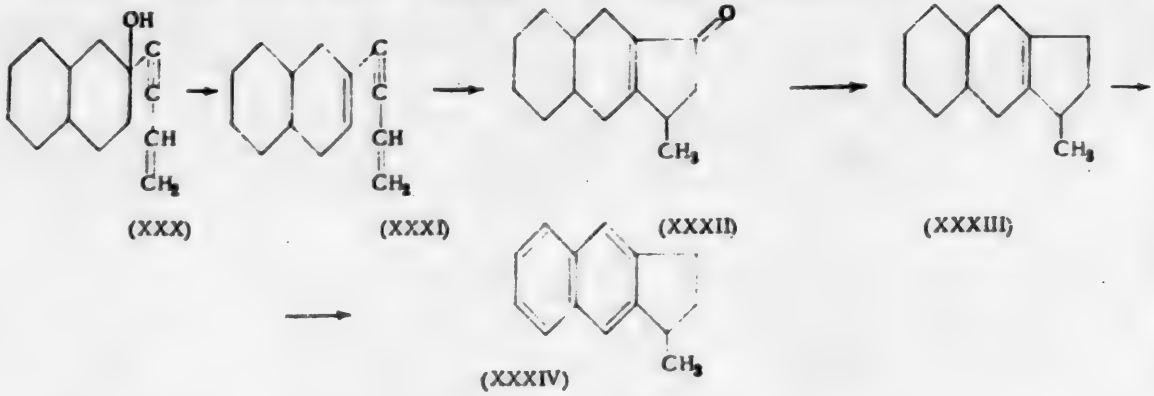


Ketone (XXII) has already been described by Mayor and Müller but they reported the incorrect melting point of 99° (instead of 71-72°) on the basis of which Barchetti [8] apparently erroneously ascribed to the product of cyclization of β-(2-naphthyl)-butyryl chloride (XXVIII) the structure of the linear ketone (XXIX) although it had the same melting point as ketone (XXII):



(XXVIII) (XXIX)

Clemmensen reduction of ketones (XXII) and (XXVI) proceeds smoothly and 60-70% yields are obtained of the corresponding hydrocarbons (XXIII) and (XXVII); the latter also gives hydrocarbon (XXIII) on dehydrogenation with palladium-on-carbon. Starting from the cis- and trans-β-vinylethinyldecalols (XXX), we also prepared the linear methylbenzindane (XXXIV) by the following route which was developed in our laboratory [9]:

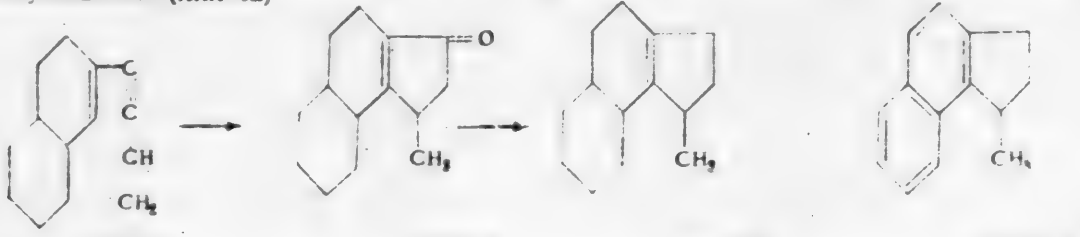


(XXX) (XXXI) (XXXII) (XXXIII)

(XXXIV)

Reduction of ketone (XXXII) by the Clemmenson method and dehydrogenation of the resultant hydrocarbon (XXXIII) to the linear methylbenzindane (XXXIV) proceed quite smoothly with yields of 80% and 60% respectively.

Dehydration of β-vinylethinyldecalol (XXX) gives, apart from the dienyne (XXXI), the dienyne (XXXV), hydration and cyclization of the latter leads to the tricyclic ketone (XXXVI). The latter is reduced with great difficulty (Clemmensen reaction) to the hydrocarbon (XXXVII) (yield about 15%), which had already failed completely to dehydrogenate to methylbenzindane (XXXVIII):

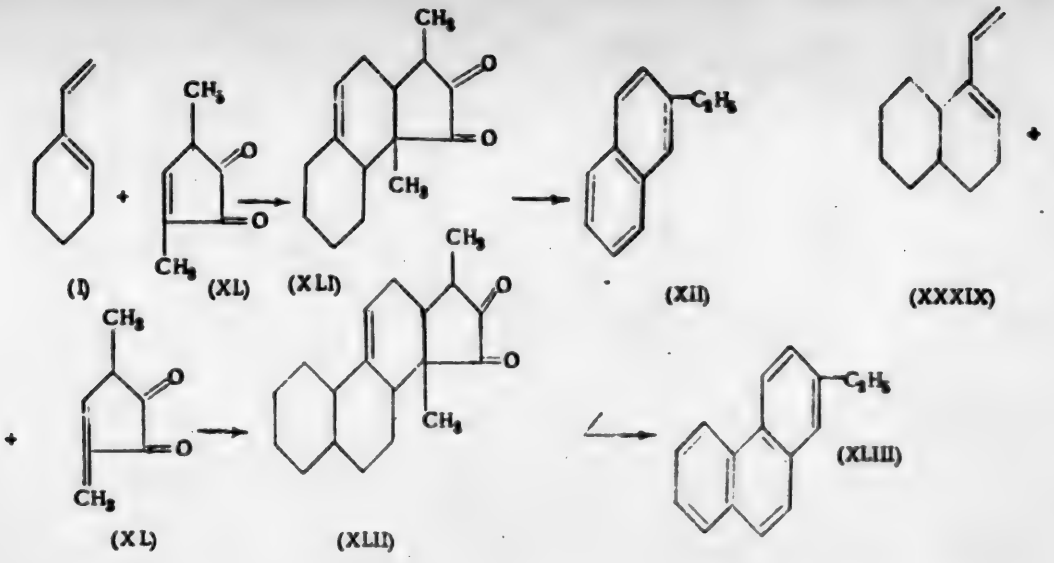


(XXXV) (XXXVI) (XXXVII) (XXXVIII)

Also proceeding according to the above-described scheme is the previously studied [10] condensation of vinylcyclohexene (I) and vinyloctaline (XXXIX) with 1,3-dimethyl-Δ⁵-cyclopenten-4,5-dione (XL). The crystalline diketones (XLI) and (XLII) are formed, the structures of which were proved by dehydrogenation with palladized carbon to respectively, 2-ethylnaphthalene (XII) and 2-ethylphenanthrene (XLIII): (see top of next page)

EXPERIMENTAL

Condensation of 1-vinyl-Δ¹-cyclohexene (I) with 1,3-dimethyl-Δ⁵-cyclopenten-5-one (II). a) 18 g 1-vinyl-Δ¹-cyclohexene (b.p. 142-144°, n_D^{20} 1.4900) and 45 g 1,3-dimethyl-Δ⁵-cyclopenten-5-one (b.p. 164-165°, n_D^{18} 1.4660) were



heated in a sealed ampoule at 125-130° for 60 hours. After distilling off the original substances, the residue was fractionated in vacuum to give 10 g of a mixture of ketones (III) and (IX) with b.p. 125-128° at 3 mm; n_D^{20} 1.5150. Repeated freezing with addition of methyl alcohol led to isolation of 8 g crystalline ketone (III) with m.p. 61-62° (from methyl alcohol), it gives a dinitrophenylhydrazone with m.p. 135-136° (from alcohol).

5.105 mg substance: 0.627 ml N_2 (23°, 752 mm). 5.310 mg substance: 0.642 ml N_2 (23° 752 mm).
Found %: N 14.00, 13.89. $C_{21}H_{24}N_4O_4$. Calculated %: N 14.07.

Ketone (III) does not form a semicarbazone even after boiling of the reactants for many hours. Ketone (III) is only hydrogenated with Pt catalyst in anhydrous acetic acid or in ethyl alcohol, but with addition in the latter case of Pd catalyst on calcium carbonate. In this process one molecule of hydrogen combines to form the saturated ketone (V) with m.p. 37-38° (from alcohol). Its 2,4-dinitrophenylhydrazone melts at 158-159° (from alcohol).

4.770 mg substance: 0.571 ml N_2 (19°, 749 mm). 4.685 mg substance: 0.563 ml N_2 (20°, 748 mm).
Found %: N 13.79, 13.78. $C_{21}H_{26}N_4O_4$. Calculated %: N 14.00.

Ketone (V) likewise fails to form a semicarbazone.

b) 19 g 1-vinyl-Δ^3-cyclohexene and 50 g 1,3-dimethyl-Δ^4-cyclopentene-5-one were heated in a sealed ampoule at 170° for 50 hours. Distillation of the original substances was followed by isolation of 12 g ketones (III) and (IX) with b.p. 137-144° at 4 mm; n_D^{20} 1.5180. Freezing yielded 7 g ketone (III) with m.p. 61-62°. The mother liquor from two experiments was combined and fractionated in vacuum to give 7 g liquid ketone (IX) with b.p. 125-127° at 4 mm; n_D^{20} 1.5175, d_4^{20} 1.018; semicarbazone with m.p. 186-187°, 2,4-dinitrophenylhydrazone with m.p. 166-167°. A mixed sample with the above-described 2,4-dinitrophenylhydrazone of ketone (III) melts at 144-150°.

Hydrogenation of ketone (IX). 6 g ketone (IX) with b.p. 125-127° at 4 mm was hydrogenated in 25 ml ethyl alcohol over Pt catalyst. 0.02 l hydrogen (1 mole) combined in a period of 2 hours. Yield 5.8 g ketone (X) with b.p. 127-129° at 4 mm; n_D^{20} 1.5098; d_4^{20} 1.010.

5.080 mg substance: 15.302 mg CO_2, 4.865 mg H_2O. Found %: C 82.20, H 10.71. $C_{15}H_{24}O$.
Calculated %: C 81.81; H 10.90.

Ketone (X) gives a 2,4-dinitrophenylhydrazone with m.p. 157-158°, a mixed sample with the above-described 2,4-dinitrophenylhydrazone of ketone (V) melts at 135-142°, i.e. a strong depression occurred. The semicarbazone of ketone (X) melts at 193-194° (from alcohol).

Isomerization of ketone (III) in the conditions of the Clemmensen reaction. A mixture of 7.8 g ketone (III) (m.p. 61-62°), 30 ml ethyl alcohol, 25 g amalgamated zinc, 20 ml water and 50 ml hydrochloric acid was boiled under a reflux condenser for 7 hours. Bath temperature 120-130°. During this period a further 60 ml hydrochloric acid was added in three portions. The product was extracted with ether, neutralized with soda, and dried with

calcium chloride. Two fractionations gave 5.1 g liquid ketone (IX) with b.p. 133-135° at 6 mm; n_D^{20} 1.5185; d_4^{20} 1.024.

9.94 mg substance: 30.00 mg CO_2; 9.33 mg H_2O. 10.58 mg substance: 31.90 mg CO_2, 9.81 mg H_2O. Found %: C 82.37, 82.28; H 10.51, 10.38. $C_{15}H_{22}O$. Calculated %: C 82.57; H 10.04.

The 2,4-dinitrophenylhydrazone melted at 165-167°.

5.588 mg substance: 0.666 ml N_2 (22°, 752 mm). 5.450 mg substance: 0.647 ml N_2 (21°, 753 mm). Found %: N 13.65, 13.66. $C_{21}H_{26}N_4O_4$. Calculated %: N 14.07.

A mixed sample with the 2,4-dinitrophenylhydrazone of the original ketone (III) melts at 128-130°.

Isomerization of ketone (III). A mixture of 5 g ketone (III) with m.p. 61-62°, 20 ml ethyl alcohol and 50 ml hydrochloric acid was refluxed in a flask at a bath temperature of 125-130° for 5 hours. The product was extracted with ether, neutralized with soda, dried with calcium chloride and fractionated in vacuum. Yield 3.5 g liquid ketone (IX) with b.p. 139-140° at 8 mm, n_D^{20} 1.5185; d_4^{20} 1.021.

12.23 mg substance. 36.76 mg CO_2; 11.32 mg H_2O. 10.51 mg substance: 31.69 mg CO_2; 9.78 mg H_2O. Found %: C 82.03, 82.28; H 10.35, 10.42. $C_{15}H_{22}O$. Calculated %: C 82.57; H 10.04.

The semicarbazone melted at 186-187°, and the 2,4-dinitrophenylhydrazone at 163-164°; they did not give a depression with the above-described semicarbazone and 2,4-dinitrophenylhydrazone of liquid ketone (IX) prepared by diene condensation of 1 vinyl-Δ^1-cyclohexene with 1,3-dimethyl-Δ^1-cyclopenten-5-one.

Reduction of ketone (III). 5 g ketone (III) with m.p. 61-62°, 40 g diethylene glycol, 20 ml ethyl alcohol and 11 ml hydrazine hydrate were refluxed on a water bath for 3 hours; 4 g KOH was then added and the heating continued with a sloping condenser for 12 hours at 200-210°. 15 ml turbid liquid distilled over. The residue was diluted with water and extracted with ether; the distillate was also extracted with ether, the ethereal solutions were combined and dried with calcium chloride. Fractionation gave: 1) a fraction with b.p. 110-150° at 6 mm; n_D^{20} 1.5140, 1 g; 2) a fraction with b.p. 160-164° at 6 mm; n_D^{20} 1.5330, 3 g.

The first and second fractions were further heated with 1 g fused KOH at 280° for 8 hours to give 0.5 g hydrocarbon (XV) with b.p. 112-114° at 7 mm, n_D^{22} 1.5140.

Reduction of ketone (V). 4.2 g ketone (V) with m.p. 36-37°, 20 ml ethyl alcohol, 40 ml diethylene glycol and 11 ml hydrazine hydrate were heated on a boiling water bath for 3 hours. Heating was then continued for 2 hours at 170-190° and 7 hours at 210-215°. The product was diluted with water, extracted with ether and dried with calcium chloride. After distilling off the ether, the residue did not distill at 7 mm and a bath temperature of 170°. 2 g fused KOH was added to it and the mixture heated at 310-320°. Vigorous evolution of nitrogen was observed and a hydrocarbon distilled over. The hydrocarbon was extracted with ether and dried with calcium chloride. Fractionation gave 1.6 g hydrocarbon (XVI) with b.p. 118-119° at 9 mm, n_D^{20} 1.5090, d_4^{20} 0.9016; MR_D 64.00, calculated 64.87.

12.37 mg substance: 39.50 mg CO_2, 13.52 mg H_2O. 12.65 mg substance: 40.33 mg CO_2, 13.98 mg H_2O. Found %: C 87.15, 87.11; H 12.23, 12.37. $C_{15}H_{24}$. Calculated %: C 87.37; H 12.63.

Dehydrogenation of hydrocarbon (XVI). a) 1.4 g hydrocarbon (XVI) (b.p. 118-119° at 9 mm, n_D^{20} 1.5090), 1.4 g palladium on carbon (5% Pd) and 15 ml benzene were heated at 360-370° for 10 hours in a metal ampoule. Fractionation gave 1 g of a mixture of products with b.p. 115-117° at 7 mm, n_D^{20} 1.5140. Judging by the refractive index, very little hydrogenation had taken place in this experiment.

b) 0.7 g hydrocarbon (XVI) from the preceding experiment with b.p. 115-117° at 7 mm was heated with 0.5 g selenium at 420° in a flask with a reflux condenser; evolution of hydrogen selenide was not observed. At a temperature of 435° a little hydrogen selenide came off and the mixture was badly resinified.

c) 1.5 g hydrocarbon (XVI) (b.p. 118-119° at 9 mm, n_D^{20} 1.5090) was passed at 360-370° for two hours through a tube packed with palladium on carbon (5% Pd). 340 ml hydrogen came off (2 moles). Fractionation gave 0.7 g hydrocarbon (XVII) or (XVIII) with b.p. 142-145° at 8 mm; n_D^{22} 1.5340.

5.147 mg substance: 16.73 mg CO_2; 4.935 mg H_2O. 8.300 mg substance: 26.930 mg CO_2; 8.023 mg H_2O. Found %: C 88.71, 88.54; H 10.73, 10.82. $C_{15}H_{22}$. Calculated %: C 89.12; H 10.89.

Dehydrogenation of ketone (III). a) 4 g ketone (III) with m.p. 61-62° and 4 g palladium-on-carbon (5% Pd) were heated in a metal ampoule for 15 minutes at 360-380°. Fractionation gave 2.5 g of a mixture of ketones with b.p. 130-132° at 3 mm; n_D^{20} 1.5310.

9.98 mg substance: 30.85 mg CO_2; 8.77 mg H_2O. 14.78 mg substance: 46.03 mg CO_2; 12.30 H_2O. Found %: C 85.21, 84.99; H 9.93, 9.77. For the original ketone (III) calculated %: C 82.57; H 10.04.

The analytical data and the index of refraction show that dehydrogenation of ketone (III) in this experiment took place to an insignificant extent.

b) 2.5 g of the mixture of ketones with b.p. 130-132° at 3 mm obtained in the preceding experiment was further heated with 2 g palladium-on-carbon (5% Pd) at 360-380° for 1½ hours. There was obtained 0.8 g hydrocarbon (XIII) with b.p. 130-134° at 4 mm; n_D^{20} 1.5780.

9.76 mg substance: 32.48 mg CO_2; 7.83 mg H_2O. 11.17 mg substance: 37.11 mg CO_2; 9.15 mg H_2O. Found %: C 90.82, 90.67; H 8.97, 9.17. $C_{15}H_{18}$. Calculated %: C 90.91; H 9.09.

c) 2.5 g ketone (III), 25 g benzene and 2 g palladium-on-carbon (5% Pd) were heated in a metal ampoule at 350-360° for 6 hours. The catalyst was filtered off and repeatedly washed with benzene. After distilling off the benzene, the product was fractionated in vacuum; first fraction b.p. 110-123° at 7 mm; n_D^{20} 1.5781, 0.5 g; second fraction b.p. 123-124° at 7 mm; n_D^{20} 1.5780, 1.25 g.

The first and second fractions were further dehydrogenated with 1 g palladium-on-carbon (5% Pd) at 350-380° for 6 hours to give 1 g fraction with b.p. 126-169° at 6 mm; n_D^{19} 1.5910. This product was again dehydrogenated with 1 g palladium on carbon (5% Pd) at 360-380° for 4 hours to give 0.6 g 1-methyl-2-isopropylnaphthalene (XIV) with b.p. 127-129° at 5 mm; n_D^{20} 1.5970; d_4^{20} 1.0137.

7.716 mg substance: 25.713 mg CO_2; 5.772 mg H_2O. Found %: C 90.94; H 8.37. $C_{14}H_{16}$. Calculated %: C 91.30; H 8.70.

The picrate melted at 99-100° (from alcohol).

4.172 mg substance: 0.381 ml N_2 (23° 739 mm) 2.451 mg substance: 0.220 ml N_2 (24°, 752 mm). Found %: N 10.24, 10.21. $C_{20}H_{19}O_7N_3$. Calculated %: N 10.16.

Oxidative cleavage of ketone (V). To 8 g ketone (V) with m.p. 37-38° and 500 ml methyl alcohol were simultaneously added, dropwise over a period of 3 hours, solutions of 32 g iodine in 480 ml methyl alcohol and 22.8 g KOH in 400 ml methyl alcohol and 80 ml water at such a rate that the iodine was in excess. On the next day the methyl alcohol was distilled off in a moderate vacuum and the residue extracted with ether for removal of the neutral products. The residue from the extraction was treated with hydrochloric acid, the acid products were extracted with ether, the ethereal solution was decolorized by shaking with concentrated sodium bisulfite solution and dried with sodium sulfate. Distillation of the ether left 6 g half-ester (VI) with m.p. 111-112° (from ligroine).

9.98 mg substance: 25.15 mg CO_2; 6.47 mg H_2O. Found %: C 68.77, H 9.48. $C_{16}H_{24}O_4$. Calculated %: C 68.08, H 9.21.

From the neutral fraction after distillation of the ether was isolated 0.6 g crystalline substance with m.p. 79-81° (from alcohol) whose structure was not established.

3.565 mg substance: 9.574 mg CO_2; 3.070 mg H_2O. 3.924 mg substance: 10.554 mg CO_2; 3.304 mg H_2O. Found %: C 73.29, 73.37; H 9.63, 9.42.

Saponification of the half-ester (VI). 5 g half ester (VI) was heated with 100 ml 10% alcoholic KOH solution for 6 hours. After distilling off the alcohol the residue was extracted with ether to remove neutral products but there was hardly a trace of these. The residue was acidified with hydrochloric acid (20 ml) and extracted with ether. From the ethereal solution was obtained 2.5 g dicarboxylic acid (VII) with m.p. 167-169° (from acetone).

9.70 mg substance: 23.85 mg CO_2, 7.80 mg H_2O. 10.28 mg substance: 25.25 mg CO_2; 8.47 mg H_2O. 0.12 g substance: 8.85 ml 0.1 N KOH. Found %: C 67.07, 67.03; H 9.09, 9.27; M 270. $C_{15}H_{24}O_4$. Calculated %: C 67.16, H 8.98; M 268.

Dehydrogenation of acid (VII). a) 1.5 g acid (VII), 10 ml benzene and 1.5 g palladium-on-carbon (5% Pd) were

heated in a metal ampoule for 7 hours at 380-390°. At the end of the reaction, the catalyst was filtered off and washed several times with benzene. The benzene was distilled off. Distillation of the residue in vacuum gave 0.5 g hydrocarbon fraction with b.p. 125-132° at 15 mm, n_D^{20} 1.5620; this gave the picrate of 1-methyl-2-ethylnaphthalene with m.p. 94-95°.

3.651 mg substance: 0.331 ml N_2 (19°, 745 mm). 5.080 mg substance: 0.461 ml N_2 (22°, 751 mm). Found %: N 10.39, 10.35. $C_{19}H_{17}O_7N_3$. Calculated %: N 10.52.

According to the literature [2], 1-methyl-2-ethylnaphthalene picrate melts at 110-111°.

b) 1.5 g acid (VII), 100 ml benzene and 3 g Raney nickel were heated at 380-390° for 25 hours. The benzene was distilled off and the residue fractionated in vacuum to give 0.3 g 2-ethylnaphthalene (XII) with b.p. 140-142° at 15 mm, n_D^{20} 1.5610; the picrate melted at 78-80°.

Oxidative cleavage of ketone (X). To 4 g ketone (X) (b.p. 127-129° at 4 mm) in 300 ml methyl alcohol were simultaneously added, over a period of 4 hours, solutions of 16 g iodine in 200 ml methyl alcohol and 11.4 g KOH in 200 ml methyl alcohol and 40 ml water at such a speed that the iodine was in excess. The next day the methyl alcohol was distilled off in vacuum, the residue was worked up with hydrochloric acid and the acid products were extracted with ether. The ethereal solution was decolorized by shaking with 5 ml concentrated sodium bisulfite solution and dried with sodium sulfate. The ether was distilled off and the product distilled in vacuum to give 5.1 g noncrystallizing half-ester (XI) which was not saponified when heated with 10% alcoholic KOH solution.

0.2268 g substance: 8.09 ml 0.1 N KOH. Found: M 280. $C_{16}H_{16}O_4$. Calculated: M 282.

Dehydrogenation of the half-ester (XI). 2.9 g half-ester (XI), 15 ml benzene and 2 g palladium-on-carbon (5% Pd), were heated at 320-340° for 5 hours. The ampoule was opened, the hydrogen released and the heating continued at 300° for 11 hours. The catalyst was filtered off, washed with benzene, the benzene was distilled off and the residue fractionated in vacuum. Yield 0.7 g of fraction with b.p. 115-120° at 5 mm, n_D^{18} 1.5630; from this was prepared the picrate of 2-ethylnaphthalene (XII) with m.p. 78-80° (from alcohol).

3.521 mg substance: 0.319 ml N_2 (22°, 752 mm) 2.351 mg substance: 0.216 ml N_2 (24°, 758 mm). Found %: N 10.38, 10.53. $C_{18}H_{15}O_7N_3$. Calculated %: N 10.90.

According to the literature [11], 2-ethylnaphthalenepicrate melts at 76-77°, and 1-ethylnaphthalene picrate melts at 98.5°.

1-Methyl-4,5-benzindane-3-one (XXII). 12.8 g naphthalene and 10.4 g crotonic anhydride (m.p. 112-114°; n_D^{20} 1.4[illegible]) were simultaneously added with energetic stirring to 30 g aluminum chloride in 100 ml carbon bisulfide. When all had been added, the mixture was stirred for 4 hours at room temperature and treated with 10% soda solution. The carbon bisulfide layer was separated and dried with calcium chloride. The residue, after distillation of the carbon bisulfide, was fractionated in vacuum to give 6.3 g ketone (XXII) with b.p. 202-204° at 15 mm and m.p. 71-72° (from carbon tetrachloride).

5.868 mg substance: 3.308 mg CO_2, 18.495 mg H_2O. 3.760 mg substance: 2.220 mg CO_2, 11.834 mg H_2O. Found %: C 85.98, 85.85, H 6.35, 6.60. $C_{14}H_{12}O$. Calculated %: C 85.71, H 6.12.

A semicarbazone could not be prepared.

1-Methyl-4,5-benzindane (XXIII). a) 4 g of the above ketone (XXII) with m.p. 71-72°, 36 ml ethyl alcohol, 15 g amalgamated zinc, 20 ml water and 50 ml hydrochloric acid were heated at 130° for 7 hours. The mixture was diluted with water, saturated with potassium carbonate and extracted with ether; the ethereal solution was dried with calcium chloride. Fractionation gave 3 g hydrocarbon (XXIII) with b.p. 133-134°, 6 mm, n_D^{18} 1.6132, d_4^{18} 1.0413.

9.93 mg substance: 33.47 mg CO_2, 6.82 mg H_2O. 9.68 mg substance: 30.64 mg CO_2, 6.24 mg H_2O. Found %: C 91.99, 92.09, H 7.73, 7.09. $C_{14}H_{14}$. Calculated %: C 92.30, H 7.70.

The picrate melted at 88-89° (from alcohol).

5.070 mg substance: 0.462 ml N_2 (19°, 745 mm) 5.340 mg substance: 0.477 ml N_2 (19°, 745 mm). Found %: N 10.44, 10.24. $C_{20}H_{17}O_7N_3$. Calculated %: N 10.21.

b) To an ethereal solution of vinylacetylene magnesium bromide prepared from 8.2 g magnesium, 41 g ethyl bromide, 25 g vinylacetylene in 320 ml ether at room temperature was added, over a period of 1½ hours, 36 g α-tetralone (b.p. 118-120° at 10 mm, n_D^{20} 1.5698) in 200 ml ether. After the whole of the ketone had been added, the mixture (pink color) was stirred for 3 hours. The next day 40 ml water and 150 ml 10% hydrochloric acid were stirred in. The ethereal solution was separated, neutralized with soda solution, washed with water and dried with magnesium sulfate. Fractionation of the reaction products in a nitrogen stream was accompanied by cleavage of water, and 17 g of a mixture of the carbinol (XXIV) and the hydrocarbon (XXV) was obtained with b.p. 126-134° at 4 mm, n_D^{16} 1.6180 [12]. The substance was heated with a mixture of 3.5 ml sulfuric acid, 10 g mercuric sulfate and 180 ml 95% methyl alcohol at 60° for 18 hours. The alcohol was distilled off in vacuum, the residue extracted with ether, the ethereal solution neutralized with soda and dried with calcium chloride. Fractionation in vacuum gave 3.5 g fraction with b.p. 184-186° at 7 mm. From two experiments were obtained 10 g of the previously described [12] crystalline ketone (XXVI) with m.p. 81-83° [contaminated with the dehydrogenated ketone (XXII)].

2.5 g ketone (XXVI) with m.p. 81-83°, 20 ml ethyl alcohol, 10 ml water, 20 ml hydrochloric acid and 12 g amalgamated zinc were heated at 120-130° for 12 hours. The mixture was extracted with ether, the ethereal solution was washed with soda solution and dried with calcium chloride. Yield 1.2 g hydrocarbon (XXVII) with b.p. 127-128° at 4 mm; n_D^{18} 1.6035. Heating of this hydrocarbon with 1 g palladium-on-carbon (5% Pd) at 360-380° for 3 hours yielded 0.65 g hydrocarbon (XXIII) with b.p. 133-134° at 4 mm; n_D^{21} 1.6120; d_4^{20} 1.037.

13.27 mg substance: 44.84 mg CO_2, 9.47 mg H_2O. 9.57 mg substance: 32.39 mg CO_2; 6.74 mg H_2O. Found %: C 92.21, 92.36; H 8.00, 7.82. $C_{12}H_{14}$. Calculated %: C 92.30; H 7.70.

The picrate melted at 87-88° and did not give a depression with the preceding specimen.

Trans-2-vinylethinyl-2-decalol (XXX). Into a three-necked round-bottomed flask fitted with a mechanical stirrer, thermometer and dropping funnel were introduced 60 g KOH and 600 ml ether. With energetic stirring and ice cooling, addition was made over a period of 2½ hours of a mixture of 92 g trans-β-decalone (b.p. 92-93° at 7 mm, n_D^{20} 1.4835), 60 g vinylacetylene and 500 ml ether. The mixture was then stirred for 4 hours. The next day 100 ml water was added to the mixture, cooled with ice water. The ethereal solution was separated, washed with 1% hydrochloric acid solution and then with water, and dried with sodium sulfate. Fractionation gave 75 g trans-2-vinylethinyl-2-decalol (XXX) with b.p. 118-122° at 4 mm, n_D^{19} 1.5250 [9].

Transformation of trans-2-vinylethinyl-2-decalol (XXX) into the tricyclic ketones (XXXII and XXXVI). 20 g of the above-described vinylacetylenic alcohol (XXX) with b.p. 118-122° at 4 mm and 20 g phosphoric acid (s.g. 1.82) were heated with stirring for 12 hours at 70°. At the end of the reaction, the mixture was diluted with double the amount of water and extracted with ether; the ethereal solution was neutralized with soda and dried with calcium chloride. Yield 11 g of a mixture of ketones (XXXII) and (XXXVI) with b.p. 145-154° at 3 mm. The mixture partly crystallized. From three such experiments was obtained 10 g of the previously described [9] crystalline ketone (XXXII) with m.p. 61-63°. From the mother liquor after separation of crystalline ketone (XXXII) was obtained 8 g liquid ketone (XXXVI) with b.p. 121-122° at 3 mm, n_D^{20} 1.5390 [9].

Reduction of ketone (XXXII). 10 g ketone (XXXII) with m.p. 61-63°, 40 g ethyl alcohol, 35 g amalgamated zinc, 15 ml water and 45 ml hydrochloric acid were heated at 125-130° for 12 hours. At the end of this period, a further 40 ml hydrochloric acid was added. The product was extracted with ether, washed with soda and dried with calcium chloride. Vacuum fractionation gave 7.5 g hydrocarbon (XXXIII) with b.p. 90-91° at 3 mm, n_D^{20} 1.5080, d_4^{20} 0.9452, MR_D 59.92, calculated 59.78.

6.100 mg substance: 6.455 mg CO_2, 19.750 mg H_2O. 5.295 mg substance: 5.690 mg CO_2; 17.140 mg H_2O. Found %: C 88.83, 88.33; H 11.85, 12.00. $C_{12}H_{20}$. Calculated %: C 88.42, H 11.56.

Dehydrogenation of hydrocarbon (XXXIII). 3.5 g hydrocarbon (XXXIII) with b.p. 90-91° at 3 mm and 1.5 g palladium on carbon (5% Pd) were heated at 370-380° for 20 hours. Yield 1.7 g 1-methyl-5,6-benzindane (XXXIV) with b.p. 118-124° at 5 mm, n_D^{18} 1.5720. The picrate melted at 115-116° (from ethyl alcohol).

3.509 mg substance: 0.314 ml N_2 (22°, 739 mm); 3.940 mg substance: 0.343 ml N_2 (20°, 739 mm). Found %: N 10.01, 9.98. $C_{18}H_{17}O_7N_3$. Calculated %: N 10.21.

Reduction of ketone (XXXVI). After two Clemmensen reductions, in the manner described above, 8 g liquid ketone (XXXVI) (b.p. 121-122° at 3 mm) gave 1.2 g hydrocarbon (XXXVII) with b.p. 112-114° at 7 mm; n_D^{20} 1.5090; d_4^{20} 0.9465; MR_D 59.93, calculated 59.78.

8.10 mg substance: 25.99 mg CO_2; 8.43 mg H_2O. 11.35 mg substance: 36.49 mg CO_2; 11.83 mg H_2O. Found %: C 87.56, 87.73; H 11.65, 11.65. $C_{14}H_{22}$. Calculated %: C 88.42; H 11.58.

Attempted dehydrogenation of this hydrocarbon with palladium-on-carbon, either in the liquid phase or in the gas phase at 360-380°, was unsuccessful.

Dehydrogenation of the tricyclic diketone (XLI). 0.5 g diketone (XLI) with m.p. 111-112°, 0.5 g palladium-on-carbon (5% Pd) and 10 ml benzene were heated for 12 hours at 350-360°. Yield 0.2 g hydrocarbon fraction from which was obtained a picrate with m.p. 78-80° (from alcohol). A mixed sample with the picrate of 2-ethylnaphthalene, prepared by dehydrogenation of the half-ester (XI), did not give a depression.

Dehydrogenation of the tetracyclic diketone (XLII). 0.5 g diketone (XLII) with m.p. 199-201°, 0.5 g palladium-on-carbon (5% Pd) and 10 ml benzene were heated at 350-360° for 8 hours. Yield 0.1 g hydrocarbon whose picrate melted at 92-94° (from alcohol).

According to the literature [13], the picrate of 2-ethylphenanthrene (XLIII) melts at 95-96°, and the picrate of 1-ethylphenanthrene at 108-109°.

SUMMARY

Diene condensation of 1-vinyl-Δ³-cyclohexene (I) with 1,3-dimethyl-Δ⁴-cyclopenten-5-one (II) gives a tricyclic ketone (III) which in the reaction conditions partly isomerizes with shift of the double bond and forms the tricyclic ketone (IX). This isomerization proceeds with particular facility on heating with hydrochloric acid. The structure of ketones (III) and (IX) was proved by their transformation into known naphthalene derivatives. A study was made of the hydrogenation, dehydrogenation and reduction (Kizhner and Clemmensen methods) of ketones (III) and (IX), as well as of the corresponding saturated ketones (V) and (X). A series of new hydrocarbons containing the benzindane skeleton was synthesized.

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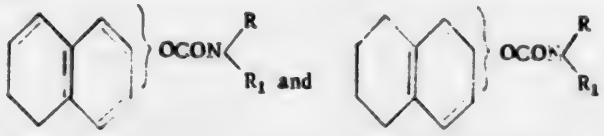
**** See Consultants Bureau English translation, page 561 ff.

***** See Consultants Bureau English translation, page 1365 ff.

N-ALKYLURETHANES AND SOME OTHER DERIVATIVES OF NAPHTHOLS AND AR-TETRALOLS

I. M. Lipovich

The purpose of the present investigation was the preparation of N-substituted urethanes of naphthols and ar-tetralols of the type of:



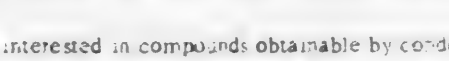
where R = R' = CH_3, C_2H_5, C_3H_7, C_4H_9, iso-C_5H_{11}, n-C_5H_{11}, $(CH_2CH_2Cl)_2$; or R = H; R' = aryl or alkyl.

The starting substances were chloroformic esters of naphthols and ar-tetraols which were obtained by reaction of a benzene solution of phosgene with the respective naphthols or ar-tetralols in presence of dimethylaniline; some of them had not previously been described in the literature. The majority of the chloroformic esters proved to be stable substances and could be isolated in the pure state. α-Tetralyl chloroformate was less stable and appreciably darkened even after keeping for a short period.

Esters of N-alkylcarbamic acids (urethanes) were obtained by condensation of chloroformates with aliphatic amines. The condensation was effected by adding a benzene solution of the chloroformate to an aqueous solution of the amine (2 moles amine to 1 mole chloroformate). In these conditions the amine hydrochloride formed at the same time as the N-alkylurethane passes into aqueous solution while the water-insolubility of the N-alkylurethane permits it to remain in solution in the benzene. Favorable conditions were thus created for the isolation of the urethanes in a sufficiently pure form. In the majority of cases the prepared urethanes were subjected to vacuum distillation, and some of them crystallized after distillation. The latter were then recrystallized. Those compounds which could not be vacuum-distilled due to decomposition were purified by recrystallization.

Apart from the above-mentioned reaction of condensation with aliphatic amines, we performed the condensation of chloroformates of α- and β-naphthols with di-(2-chloroethyl)-amine, condensation conditions being found that enabled the yield of the corresponding urethanes to reach 80% of theory (for details see the experimental part).

We were also interested in compounds obtainable by condensation of chloroformates of ar-tetralols with anthranilic acid. With this objective we prepared apart from the known 5 tetrahydronaphthyl ester of 2-carboxyphenylcarbamic acid [1], the previously undescribed α-tetrahydronaphthyl ester of 2 carboxyphenylcarbamic acid:



We also describe the α- and β-tetrahydronapthyl esters of phenylcarbamic acid since we were unable to find these compounds described in the literature. Their preparation with the help of phenylisocyanate was considerably accelerated by addition of a trace of aluminium chloride. All the derivatives of N-substituted carbamic acids that we prepared were sparingly soluble in water and very readily soluble in organic solvents. An attempt to increase the solubility in water of these compounds by preparing their salts was unsuccessful.

We also prepared the benzyl ethers of ar-tetralols by reaction of an alcoholic alkaline solution of ar-tetralols with an alcoholic solution of benzyl chloride. The benzyl ethers of ar-tetralols are high boiling liquids which darken on standing.

EXPERIMENTAL

General Method of Preparation of N-alkylurethanes of Naphthols and ar-Tetralols

a) Preparation of chloroformates of naphthols and tetralols. To a 15% benzene solution of phosgene was

gradually added, with cooling and mechanical stirring, the appropriate naphthol or tetralol dissolved in a mixture of benzene and dimethylaniline. After the solution had been added, stirring was continued for an hour at room temperature. A precipitate soon appeared, dimethylaniline hydrochloride. The substances were taken in the following proportions: 1.2 moles phosgene and 1 mole dimethylaniline per mole of naphthol or tetralol. The reaction mixture was left overnight, the next day 10% hydrochloric acid was added to the cooled solution and the aqueous layer containing the dimethylaniline hydrochloride was separated. The benzene solution, containing the chloroformate of the naphthol or tetralol, was washed with water and dried with sodium sulfate. The benzene was distilled off in vacuum and then the residue distilled in vacuum.

b) Condensation of chloroformates of naphthols and tetralols with amines. To an aqueous solution of the amine is gradually added, with cooling and mechanical stirring, a benzene solution of the chloroformate of the naphthol or the tetralol. In the majority of cases the chloroformates were used without isolating them in the pure form, i.e. they were used in the form of the benzene solution prepared as described above.

In our investigation we used mainly 50% aqueous solutions of amines (in isolated cases, 20%), for example in condensation with dimethylaniline; sometimes we used benzene solutions of amines, e.g. in condensation with n-butylamine.

After the addition of the chloroformate of the naphthol or tetralol, stirring is continued at room temperature for 2 - 2½ hours. The aqueous layer is separated from the benzene layer. The benzene solution is washed several times with water and dried with sodium sulfate before the benzene is distilled in vacuum. The residue is distilled in vacuum. A second distillation was occasionally carried out. When crystalline compounds were formed, these were recrystallized. 2 moles amine were taken per mole ester in condensation of chloroformates of naphthols and tetralols.

I. Chloroformates of Naphthols and Tetralols

1. α-Naphthyl Chloroformate: a liquid with b.p. 139-140° at 7-8 mm.

5.530 mg substance: 3.812 mg AgCl. 6.025 mg substance: 4.120 mg AgCl. 5.883 mg substance: 13.750 mg CO_2, 1.851 mg H_2O. Found %: Cl 17.05, 16.89, C 63.74, H 3.52. $C_{11}H_7O_2Cl$. Calculated %: Cl 17.19, C 63.92, H 3.39.

2. β-Naphthyl Chloroformate:* b.p. 146-147° at 8-9 mm. Rapidly crystallizes. M.p. 60-62° (from hexane).

4.368 mg substance: 3.070 mg AgCl. 6.000 mg substance: 4.170 mg AgCl. Found %: Cl 17.40, 17.19. $C_{11}H_7O_2Cl$. Calculated %: Cl 17.19.

3. α-Tetralyl Chloroformate: liquid with b.p. 143° at 12 mm. Darkens on standing.

4. β-Tetralyl Chloroformate:** Liquid with b.p. 133-134° at 7-8 mm.

3.660 mg substance: 8.451 mg CO_2, 1.670 mg H_2O. 8.574 mg substance: 5.813 mg AgCl. Found %: C 62.97, H 5.11, Cl 16.77. $C_{11}H_{11}O_2Cl$. Calculated %: C 62.70, H 5.22, Cl 16.86.

II. N-Alkyl- and N-Acyl Urethanes of Naphthols and ar-Tetralols

1. α-Naphthyl Dimethylcarbamate $\alpha\text{-}C_{10}H_7OCON(CH_3)_2$.

B.p. 191-192° at 11-12 mm. It crystallizes after lengthy standing (1 - 1½ months). Crystallization sets in rapidly after seeding. M.p. 52-55° (from ligroine). Colorless crystals, insoluble in water, soluble in organic solvents.

5.020 mg substance: 13.435 mg CO_2, 2.745 mg H_2O. 4.693 mg substance: 12.543 mg CO_2, 2.577 mg H_2O. 9.600 mg substance: 0.577 ml N_2 (20°, 730 mm). Found %: C 72.92, 72.90, H 6.12, 6.14; N 6.68. $C_{13}H_{13}O_2N$. Calculated %: C 72.55, H 6.05, N 6.50.

2. α-Naphthyl Diethylcarbamate.

From 16 g α-naphthol is obtained 23 g substance with b.p. 201-202° at 10-11 mm. Crystallizes quickly. Two recrystallizations from hexane give faintly colored crystals with m.p. 59-61°. Insoluble in water, very readily

* This chloroformate was previously prepared in presence of quinoline [2] with m.p. 65-66°, and in presence of dimethylaniline [3] with m.p. 57°.

** β-Tetralyl chloroformate is mentioned in the patent literature but without indication of its constants and analysis.

soluble in alcohol, ligroine and hexane.

3.619 mg substance: 9.853 mg CO_2; 2.277 mg H_2O. 3.107 mg substance: 8.417 mg CO_2; 1.885 mg H_2O. 4.578 mg substance: 1.90 ml 0.01 N H_2SO_4 for combining with the NH_3. Found %: C 74.25, 73.88; H 7.04, 6.79; N 5.81. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

3. α-Naphthyl n-Dipropylcarbamate.

A liquid with b.p. 201-202° at 7 mm was obtained. Insoluble in water, readily soluble in organic solvents. Yield 65% of theory.

5.218 mg substance: 14.413 mg CO_2; 3.610 mg H_2O. 12.911 mg substance: 4.66 ml 0.01 N H_2SO_4 for combining with NH_3. Found %: C 75.33; H 7.74; N 5.06. $C_{16}H_{21}O_2N$. Calculated %: C 75.27; H 7.75; N 5.16.

4. α-Naphthyl n-Dibutylcarbamate.

From 18.5 g α-naphthol is obtained 25 g substance with b.p. 235-237° at 10 mm. Insoluble in water, readily soluble in organic solvents.

5.196 mg substance: 14.376 mg CO_2; 3.900 mg H_2O. 7.715 mg substance: 2.62 ml 0.01 N H_2SO_4 for combining with NH_3. Found %: C 75.45; H 8.40; N 4.75. $C_{18}H_{25}O_2N$. Calculated %: C 75.79; H 8.07; N 4.91.

5. α-Naphthyl n-Butylcarbamate $\alpha\text{-}C_{10}H_7OCONH(C_4H_9)$.

In this case the benzene solution of α-naphthyl chloroformate is first dried thoroughly and then condensed with the benzene solution of n-butylamine. After removal of the n-butylamine hydrochloride, the benzene solution is evaporated to dryness in vacuum. The residue is recrystallized from alcohol. From 9 g α-naphthyl chloroformate is obtained 4.1 g substance. Faintly colored crystals in the form of prisms with m.p. 69-72°. Insoluble in water, readily soluble in organic solvents.

4.340 mg substance: 11.749 mg CO_2; 2.853 mg H_2O. 3.882 mg substance: 10.508 mg CO_2; 2.504 mg H_2O. 5.960 mg substance: 0.317 ml N_2 (27°, 730 mm). 7.390 mg substance: 0.392 ml N_2 (27°, 730 mm). Found %: C 73.83, 73.82; H 7.35, 7.21; N 5.81, 5.79. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00, N 5.76.

6. α-Naphthyl Diisoamylcarbamate.

The compound was prepared by the general method, but after condensation of the α-naphthyl chloroformate with the aqueous solution of diisoamylamine, the sparingly-soluble diisoamylamine hydrochloride is precipitated. Consequently prior to separation of the aqueous layer from the benzene layer, the diisoamylamine hydrochloride is removed. Further working up is by the general method. Two vacuum distillations gave a substance with b.p. 226-227° at 6 mm. Yield 70% of theory.

6.299 mg substance: 17.748 mg CO_2; 4.837 mg H_2O. 4.[illegible] mg substance: 1.24 ml 0.01 N H_2SO_4 for combining with NH_3. Found %: C 76.85; H 8.59; N 4.17. $C_{20}H_{29}O_2N$. Calculated %: C 77.06; H 8.87; N 4.28.

7. α-Naphthyl n-Diamylcarbamate.

Reaction conditions and procedure for separation were the same as in the preceding experiment. The pale-green product had b.p. 224-225° at 6 mm. Yield 60% of theory.

5.944 mg substance: 16.769 mg CO_2; 4.680 mg H_2O. 10.750 mg substance: 0.410 ml N_2 (30°, 733 mm). Found %: C 76.94; H 8.82; N 4.26. $C_{20}H_{29}O_2N$. Calculated %: C 77.06; H 8.87; N 4.28.

8. α-Naphthyl Di-(2-chloroethyl)carbamate $\alpha\text{-}C_{10}H_7OCON(CH_2CH_2Cl)_2$.

10 g di-(2-chloroethyl)amine hydrochloride is dissolved in 20 ml water and stirred with an aqueous solution of alkali (2.3 g NaOH in 15 ml water) at 0°. To the resultant solution of di-(2-chloroethyl)amine are gradually added simultaneously in the course of an hour, with good mechanical stirring and cooling to 0-5°, a chloroform solution of α-naphthyl chloroformate (11.17 g ester in 18 ml chloroform) and an alkali solution (2.5 g NaOH in 25 ml water). The chloroform solution is then separated from the aqueous layer. The chloroform is driven

off. The residue is distilled in vacuum. A product is obtained with b.p. 222-223° at 4-3 mm and very quickly crystallizing. Yield 16 g or 80% of the theoretical. After recrystallization from alcohol the m.p. is 81-83°. Colorless crystals, insoluble in water, soluble in organic solvents.

3.441 mg substance: 7.286 mg CO_2; 1.595 mg H_2O. 3.124 mg substance: 6.600 mg CO_2; 1.435 mg H_2O. 7.930 mg substance: 0.318 ml N_2 (24.0°, 728 mm). 8.620 mg substance: 0.336 ml N_2 (24.0°; 728 mm). 6.034 mg substance: 5.439 mg AgCl. Found %: C 57.74, 57.62; H 5.18, 5.14; N 4.41, 4.29; Cl 22.30. $C_{15}H_{15}O_2NCl_2$. Calculated %: C 57.69; H 4.80; N 5.49; Cl 22.75.

9. β-Naphthyl Dimethylcarbamate. •

Prepared by the general method. A 20% aqueous solution of dimethylamine was taken for the reaction. After the solvent had been driven off in vacuum, the residue crystallized. M.p. 96-98° after 3 recrystallizations from alcohol. Colorless crystals, insoluble in water, readily soluble in organic solvents.

4.011 mg substance: 10.723 mg CO_2; 2.257 mg H_2O. 7.00 mg substance: 0.397 ml N_2 (20°, 743 mm). Found %: C 72.91; H 6.29, N 6.42. $C_{13}H_{13}O_2N$. Calculated %: C 72.55; H 6.05; N 6.50.

10. β-Naphthyl Diethylcarbamate.

The compound has b.p. 203-205° at 11 mm. Rapidly crystallizes. M.p. 56-58° after two recrystallizations from hexane. Colorless crystals, insoluble in water, very easily soluble in organic solvents. Yield 70% of theory.

4.420 mg substance: 11.948 mg CO_2; 2.770 mg H_2O. 3.882 mg substance: 10.501 mg CO_2, 2.395 mg H_2O. 6.890 mg substance. 2.85 ml 0.01 N H_2SO_4, for combining with NH_3. 6.834 mg substance: 2.81 ml 0.01 N H_2SO_4, for combining with NH_3. Found %: C 73.72, 73.77; H 7.01, 6.90; N 5.79, 5.75. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

11. β-Naphthyl n-Butylcarbamate β-$C_{10}H_7OCONH(C_4H_9)$.

Prepared in the conditions described above for α-naphthyl n-butylcarbamate. The compound is first recrystallized from a mixture of ligroine and benzene, and then from alcohol, m.p. 121-123°, forms platelets, insoluble in water, readily soluble in organic solvents.

3.772 mg substance: 10.288 mg CO_2; 2.471 mg H_2O. 3.710 mg substance: 10.059 mg CO_2; 2.379 mg H_2O. 8.320 mg substance: 0.431 ml N_2 (27.0°, 729 mm). 6.285 mg substance: 0.327 ml N_2 (25.5°, 730 mm). Found %: C 74.38, 73.95; H 7.33, 7.17; N 5.66, 5.72. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 7.00; N 5.76.

12. β-Naphthyl Di-(2-chloroethyl)carbamate.

The reaction was performed and the compound worked up as in the case of α-naphthyl di-(2-chloroethyl)carbamate. A compound was obtained with b.p. 233-237° at 3 mm. On recrystallization from alcohol it formed small needles with m.p. 65-68°. Yield 60% of theory.

3.985 mg substance: 8.371 mg CO_2; 1.645 mg H_2O. 7.635 mg substance: 0.312 ml N_2 (24°, 728.5 mm). 7.565 mg substance: 0.310 ml N_2 (24.0°, 728.5 mm). 4.855 mg substance: 4.385 mg AgCl. Found %: C 57.28, H 4.62, N 4.50, 4.52, Cl 22.34. $C_{15}H_{15}O_2NCl_2$. Calculated %: C 57.69; H 4.80, N 4.49, Cl 22.75.

13. α-Tetrahydronaphthyl Diethylcarbamate ar-α-$C_{10}H_{11}OCON(C_2H_5)_2$.

Liquid with b.p. 191-192° at 13 mm. Yield 70% of the theoretical.

3.070 mg substance: 8.218 mg CO_2; 2.309 mg H_2O. 7.385 mg substance: 0.370 ml N_2 (22°, 733 mm). Found %: C 73.01; H 8.42, N 5.59. $C_{15}H_{21}O_2N$. Calculated %: C 72.87; H 8.50, N 5.67.

14. α-Tetrahydronaphthyl n-Dibutylcarbamate.

From 18.5 g α-tetralol was obtained 20 g substance with b.p. 215-217° at 8 mm.

• Previously obtained by reacting trimethylamine with β-naphthyl chloroformate [3] m.p. 92°.

5.084 mg substance: 14.100 mg CO_2; 4.237 mg H_2O. 15.020 mg substance: 0.849 ml N_2 (21°; 726.5 mm). Found %: C 75.63; H 9.32; N 4.75. $C_{14}H_{19}O_2N$. Calculated %: C 75.25; H 9.57; N 4.62.

15. β-Tetrahydronaphthyl Diethylcarbamate.

Liquid with b.p. 192-194° at 8-9 mm. It crystallizes on standing, but sometimes the process of crystallization continues for several weeks. After two recrystallizations from alcohol it forms colorless crystals with m.p. 62-64°.

3.806 mg substance: 10.239 mg CO_2; 2.882 mg H_2O. 5.302 mg substance: 2.12 ml 0.01 N H_2SO_4 required for combining with the NH_3. Found %: C 73.36; H 8.47; N 5.60. $C_{15}H_{21}O_2N$. Calculated %: C 72.87; H 8.50; N 5.67.

16. α-Tetrahydronaphthyl 2-Carboxyphenylcarbamate, α-$C_{10}H_{11}OCONH$-C$_6$H$_4$-COOH

To a benzene solution containing α-tetralyl chloroformate (prepared from 50 g α-tetralol by the above-described method) is added, with cooling and stirring, 46 g anthranilic acid. After the acid has been added, stirring is continued for several hours at room temperature and the mass is left till the next day. An aqueous solution of KOH (10 g KOH in 100 ml water) is then added, with cooling and mechanical stirring, and stirring afterwards continued for several hours. The precipitate is filtered, washed several times with hot water. After two recrystallizations from alcohol a substance with m.p. 167-169° (with decomposition) is obtained. Insoluble in water, soluble in alcohol, acetone and chloroform.

3.583 mg substance: 9.128 mg CO_2; 1.796 mg H_2O. 3.742 mg substance: 9.530 mg CO_2; 1.820 mg H_2O. 8.668 mg substance: 0.367 ml N_2 (27.5°, 724 mm). 8.397 mg substance: 0.351 ml N_2 (26°, 724 mm). Found %: C 69.48, 69.46; H 5.60, 5.45; N 4.58, 4.58. $C_{24}H_{21}O_4N$. Calculated %: C 69.45; H 5.46; N 4.50.

17. α-Tetrahydronaphthyl Phenylcarbamate, α-$C_{10}H_{11}OCONH(C_6H_5)$.

To 20 g α-tetralol is added 20 g phenylisocyanate, solution is effected by heating, and the mass is left at room temperature for 7 days; the precipitate is then drained and washed several times with ligroine. Two recrystallizations (from alcohol-acetone and then from acetone) gave 10 g with m.p. 169-171°; fine crystals in form of needles.

3.561 mg substance: 9.998 mg CO_2; 2.015 mg H_2O. 6.674 mg substance: 0.315 ml N_2 (23°, 729 mm). 7.205 mg substance: 0.347 ml N_2 (23°, 729 mm). Found %: C 76.57; H 6.33; N 5.22, 5.33. $C_{17}H_{17}O_2N$. Calculated %: C 76.40; H 6.36; N 5.24.

18. β-Tetrahydronaphthyl Phenylcarbamate.

To 25 g β-tetralol is added 25 g phenylisocyanate, solution is effected by heating, and addition is then made of a trace of aluminum chloride. Crystallization is complete after a day. The crystals are drained and washed with ligroine. Yield 40 g unpurified substance. M.p. 151-152° after three recrystallizations from acetone; white needles.

3.065 mg substance: 8.600 mg CO_2; 1.725 mg H_2O. 8.035 mg substance: 0.388 ml N_2 (22.5°, 741 mm). 7.145 mg substance: 0.333 ml N_2 (22.5°, 743.5 mm). Found %: C 76.51; H 6.30; N 5.44, 5.27. $C_{17}H_{17}O_2N$. Calculated %: C 76.40; H 6.36; N 5.24.

19. α-Tetralyl-benzyl Ether, α-$C_{10}H_{11}OCH_2C_6H_5$.

To 9.3 g KOH in 40 ml absolute alcohol is added 22.2 g α-tetralol with heating. Gradual addition is then made to the solution of an alcoholic solution of benzyl chloride (38 g benzyl chloride in 40 ml alcohol). Heating is then continued for 2½ hours. After cooling, the KCl is filtered off. The alcohol is driven off and the residue is diluted with water and extracted with ether. The ether extract is washed several times with Claisen mixture and then with water and dried with calcium chloride.

The ether is driven off and the residue distilled in vacuum. The benzyl ether of α-tetralol forms a light-yellow liquid with b.p. 195-196° at 9 mm. Color changes to cherry-red on standing. Analysis for hydroxyl group gave a negative result.

3.500 mg substance: 11.038 mg CO_2; 2.305 mg H_2O. Found %: C 86.01; H 7.36. $C_{17}H_{18}O$. Calculated %: C 85.71; H 7.56.

20. β-Tetralyl Benzyl Ether.

Prepared in the above-described conditions for the benzyl ether of α-tetralol. The benzyl ether of β-tetralol is a liquid with b.p. 169-171° at 5-6 mm, insoluble in water, easily soluble in organic solvents.

4.195 mg substance: 13.215 mg CO_2; 2.784 mg H_2O. 3.624 mg substance: 11.435 mg CO_2; 2.411 mg H_2O. Found %: C 85.91, 86.05; H 7.43, 7.44. $C_{17}H_{18}O$. Calculated %: C 85.71; H 7.56.

SUMMARY

Condensation of chloroformates of naphthols and ar-tetralols with aliphatic amines yielded a series of their N-alkyurethanes not previously described in the literature. Several other derivatives of naphthols and ar-tetralols, likewise undescribed in the literature, were also prepared.

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[2] Ann., 382, 256.

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THE PROBLEM OF THE SYNTHESIS OF SUBSTITUTED CYSTEINES

II. THE POSSIBILITY OF FUSING SUBSTITUTED HYDANTOINS FOR THE PREPARATION OF β,β-DIPHENYLCYSTEINE

T. A. Favorskaya and L. A. Remizova

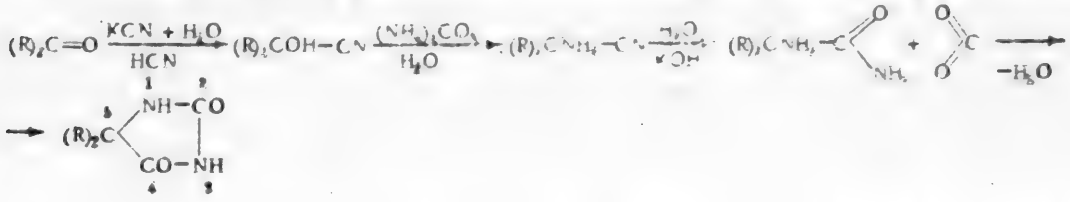
In the first communication [1], it was shown that the reaction of diphenylacetaldehyde and diphenylglycolaldehyde with KCN and NH_4Cl in aqueous ethereal solution proceeds mainly with formation of hydroxy- and dihydroxynitriles, the yield of the corresponding amino- and hydroxyaminonitriles being very small. Moreover, hydrolysis of the isolated hydrochloride of α-amino-β,β-diphenylpropionitrile showed that this compound is very unstable and readily undergoes – both in an acid and an alkaline medium – various transformations, leading to shortening of the chain of carbon atoms, to formation of simpler compounds (benzhydrol, diphenylacetaldehyde and diphenylacetic acid). An attempt was therefore made to prepare α-amino-β,β-diphenylpropionic acid by another route.

One of the methods of synthesis of α-amino acids is the hydrolysis of the corresponding substituted hydantoins.

In 1934 Bucherer and co-workers [2, 3] developed a method of preparation of hydantoins, starting from aldehydes and ketones which were reacted with KCN and ammonium carbonate in aqueous alcoholic medium. By replacing the aldehydes by their bisulfite derivatives, the authors avoided the resinification which usually occurs when the reaction is carried out with the aldehydes themselves. The authors believe that hydantoins are formed via the following series of intermediates: hydroxynitrile, aminonitrile, and carbamic acid; the latter is unstable and undergoes intramolecular rearrangement at the instant of its formation, into another unstable compound which in turn rearranges into the stable hydantoin.

Other authors [4] had investigated the preparation of various hydantoins by a similar method about the same time as Bucherer, but using a higher temperature and a pressure of 2-8 atmospheres. They believe that the carbonyl compound reacts with KCN and ammonium carbonate in its enol form. Their reason for so thinking is that ketones whose carbonyl group is linked to two aromatic radicals, e.g. benzophenone, are recovered unchanged in this reaction, whereas benzylphenyl ketone – which is capable of enolization – forms an hydantoin with good yield. Recently, however, conditions were established [5] for the preparation from diaryl ketones of the corresponding 5,5-diarylhydantoins in over 90% yield; this shows that enolization is not an essential condition for reaction of carbonyl compounds with potassium cyanide.

The formation of a hydantoin may be explained more simply by assuming that the initially formed aminonitrile hydrolyzes in an alkaline medium to the amino acid amide, which reacts with CO_2 to form the hydantoin

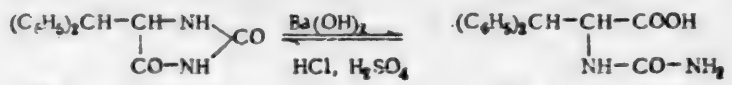


In recent years investigators have shown greatly increased interest in the synthesis of hydantoins because some of these, for example, 5,5-ethylphenylhydantoin (nirvanol) and 5,5-diphenylhydantoin (dilantin) possess an anticonvulsant activity and are used for treatment of epilepsy [6]. Moreover, substituted hydantoins serve as a source of α-amino acids, formed as a result of their hydrolysis. However, the hydrolysis of hydantoins is not so simple because hydantoins are stable toward dilute acids: even boiling concentrated hydrochloric acid has no action on them, and 40% sulfuric acid only partly hydrolyzes them. Complete hydrolysis can only be effected with 60% sulfuric acid by heating to 120-130° [2]. In this way Bucherer succeeded in preparing the corresponding amino acids from 5,5-dimethyl- and 5-methyl-5-ethylhydantoins.

Heating of hydantoins with dilute caustic alkalies [7] brings about hydration of the ring and formation of hydantoic acid. From the latter the hydantoins can be regenerated by heating with dilute mineral acids [8]. Sometimes a hydantoic acid can be converted into an amino acid; thus, N. A. Menshutkin [9] obtained glycine by heating hydantoic acid in a sealed tube with hydriodic acid for 20 hours at 160-170°. The best method of hydrolysis of hydantoins—and the one in use at the present time—is heating of hydantoins with barium hydroxide in aqueous solution in a sealed tube. By this method hydantoins have been converted into such amino acids as lysine $NH_2-(CH_2)_4-CHNH_2-COOH$ [10,11], serine $HOCH_2-CH(NH_2)-COOH$, cysteine $HS-CH_2-CH(NH_2)-COOH$ [12], methionine [13] $CH_3SCH_2-CH_2-CH(NH_2)COOH$, etc.

After failing to prepare α-amino-β,β-diphenylpropionic acid by the action of KCN and NH_4Cl on diphenylacetaldehyde, we decided to attempt to prepare this acid by hydrolysis of 5-benzhydrylhydantoin (I). This hydantoin was prepared in 1960 [6] in 44% yield by the reaction of diphenylacetaldehyde with KCN and ammonium carbonate when heated at 110° under pressure. The author prepared diphenylacetaldehyde by a rather complex method starting from formaldehyde.

We prepared the hydantoin in 75% yield by Bucherer's method [2,3]. Heating of the hydantoin with 60% sulfuric acid at 130-140° for an hour had no result apart from formation of resins. The hydantoin was recovered unchanged after prolonged boiling with concentrated hydrochloric acid, as well as after boiling with hydriodic acid in presence of acetic anhydride [12]. Boiling of the hydantoin with an aqueous solution of barium hydroxide at atmospheric pressure resulted in a quantitative yield of the previously unknown α-benzhydrylhydantoic acid (II). Heating of the hydantoin with barium hydroxide in a sealed tube at 140° for 15 minutes gave the same hydantoic acid but in lower yield; α-benzhydrylhydantoic acid is quantitatively reconverted into the hydantoin when heated with dilute and concentrated hydrochloric acid or with dilute sulfuric acid.



(I) (II)

Although we thus failed to obtain α-amino-β,β-diphenylpropionic acid from 5-benzhydrylhydantoin we decided to attempt to introduce the sulfhydryl group into the 5-benzhydrylhydantoin molecule and thereby to obtain the mercaptohydantoin and therefrom the mercaptohydantoic acid. It should be interesting to prepare such compounds from the standpoint of their pharmacological properties. With this aim, it was decided to prepare mercaptodiphenylacetaldehyde and to convert this into the hydantoin.

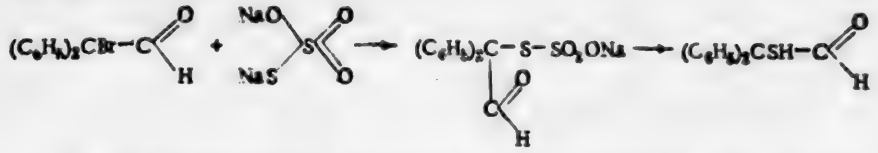
Introduction of the mercapto group into the molecule of an aliphatic compound is usually effected by reacting hydrosulfides of alkali metals with halogen derivatives of these compounds [14, 15, 16, 17]. V. M. Rodionov [18] however recommends treating benzyl chloride with sodium thiosulfate in aqueous alcoholic solution to form benzylmercaptan. The reaction proceeds with formation of the intermediate known as Bunte's salt treatment of which with dilute sulfuric acid decomposes it to benzylmercaptan.

We resolved to apply this method to the preparation of mercaptodiphenylacetaldehyde. The substance obtained by this reaction was distilled in high vacuum. Its color was emerald green, it had a repulsive, clinging odor, the reaction to litmus was neutral, and it gave a positive reaction for sulfur. On standing, the color gradually changed from deep-green to light yellow and the reaction to litmus changed from neutral to acid. Moreover, the substance gave a positive reaction for the aldehyde group, but a qualitative test for the mercapto group with nascent nitrous acid was negative; the substance did not titrate with iodine. Quantitative analysis for sulfur (Carius) gave only a 2% content in place of the 14% calculated for mercaptodiphenylacetaldehyde. Treatment with 2,4-dinitrophenylhydrazine gave two 2,4-dinitrophenylhydrazones, one with m.p. 237° (the 2,4-dinitrophenylhydrazone of benzophenone) and one with m.p. 145-146° (the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde).

On the basis of these data we may say that although the substance distills within a range of one degree, it is a mixture of which one of the components is benzophenone. It was impossible to judge whether the other substance was diphenylacetaldehyde or thiodiphenylacetaldehyde or a mixture of these, on the basis solely of preparation of the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde because both aldehydes give one and the same 2,4-dinitrophenylhydrazone. The presence of the thioaldehyde was inferred from the emerald color and the very repulsive odor. Moreover, the development of an acid reaction and the color change on standing pointed to the easy oxidizability of the substance, which is characteristic of thioaldehydes.

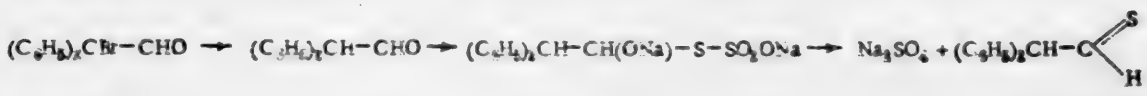
We know [19] that aldehydes can react with sodium thiosulfate not only with formation of mercapto derivatives; in an anhydrous medium they react to form thioaldehydes. In our case, evidently, the reaction of bromodiphenylacetaldehyde with sodium thiosulfate proceeded in several directions.

On the one hand the reaction probably proceeded, according to Rodionov's mechanism, with formation of the mercaptoaldehyde:



The mercaptoaldehyde decomposed into thiobenzophenone and formaldehyde, while the thiobenzophenone (readily oxidizable in the air) gave benzophenone which was detected in the reaction products.

At the same time the sodium thiosulfate acted on the bromodiphenylacetaldehyde as a reducing agent and transformed it into diphenylacetaldehyde, whose aldehyde group entered into reaction with $Na_2S_2O_3$ to form the thioaldehyde:



This second direction of the reaction accounts for the presence of diphenylacetaldehyde and thiodiphenylacetaldehyde in the reaction products.

After failing to obtain the mercaptoaldehyde by Rodionov's method, we decided to attempt its preparation by the action of NaSH on bromodiphenylacetaldehyde in an anhydrous medium. With this objective, freshly prepared sodium hydrosulfide, suspended in dry benzene, was slowly stirred into a benzene solution of bromodiphenylacetaldehyde. The reaction was performed at room temperature. Addition of the hydrosulfide was accompanied by release of heat and development of a dark blue color. The reaction product was distilled in high vacuum to give a liquid with a blue color and a neutral reaction to litmus. The blue color disappeared fairly quickly on standing; the product did not have a repulsive odor and did not give a reaction for sulfur. Treatment with 2,4-dinitrophenylhydrazine gave two 2,4-dinitrophenylhydrazones corresponding to derivatives of benzophenone and diphenylacetaldehyde. These results showed that in this case also the bromodiphenylacetaldehyde had been partly reduced to diphenylacetaldehyde. The formation of benzophenone in both cases shows that (in both cases) there is, so to speak, partial replacement of bromine in bromodiphenylacetaldehyde by the mercapto group, but in the reaction conditions the mercaptodiphenylacetaldehyde is unstable and behaves like the derivatives of diphenylglycolaldehyde and diphenylacetaldehyde that we have previously studied [9] in decomposing with formation of thiobenzophenone, which oxidizes to benzophenone in the air. The deep blue color, characteristic of thioketones, is indicative of the presence of thiobenzophenone in the reaction products.

EXPERIMENTAL

Preparation of 5-Benzhydrylhydantoin

In a round-bottomed flask are placed 22 g KCN (2 moles), 64 g ammonium carbonate (4 moles) and 200 ml 50% ethyl alcohol. Gradual addition is then made, with stirring, of 40 g of the bisulfite derivative of diphenylacetaldehyde. The reaction mixture is heated on the water bath so that the temperature in the flask is 50-55°; after 6 hours' heating at this temperature the temperature is raised to 70-75° to decompose the excess of ammonium carbonate. After cooling of the solution the formed hydantoin crystallizes. The filtered hydantoin is washed with water to remove inorganic impurities. Weight of the hydantoin 14 g. The filtrate deposited a further 11.3 g on standing. M.p. 218-219° from aqueous alcohol. Yield 26.2 g or 74%.

According to the literature the m.p. is 221°.

0.0738 g substance: 6.8 ml N_2 (15°, 754.9 mm). 0.1595 g substance: 11.98 g dioxane: Δt 0.315°.
Found %: N 10.65; M 234.6. $C_{16}H_{14}O_2N_2$. Calculated %: N 10.52; M 266.

Due to the insolubility of the prepared hydantoin in benzene, the molecular weight was determined in dioxane, the dioxane constant for phenylacetic acid was previously determined.

Hydrolysis of 5-Benzhydrylhydantoin

2.5 g 5-benzhydrylhydantoin was heated with 100 ml 60% sulfuric acid for an hour at 120-130°. After cooling, the sulfuric acid was neutralized with the calculated amount of $BaCO_3$, the precipitate was filtered and washed with ether. Removal of the ether left a small amount of resin. The aqueous solution had the mousy odor characteristic of acetamide, but no organic products whatever could be isolated from it. In the specified conditions, therefore, the 5-benzhydrylhydantoin had decomposed. When the reaction was performed in milder conditions (heating at 100°) the hydantoin was recovered unchanged.

2 g hydantoin was heated with 8 g $Ba(OH)_2 \cdot 8H_2O$ and 50 ml water in a sealed tube for 15 minutes at 136°. After opening the tube, the inorganic precipitate was filtered off and the filtrate was acidified with dilute hydrochloric acid until weakly acid; a substance was precipitated which gave a positive reaction for nitrogen, had an acid reaction, and melted at 178-180° before recrystallization. From the residual solution was isolated a small amount of neutral product of decomposition not containing nitrogen and melting at 74-76°; it was not further investigated. In the next experiment, in order to avoid decomposition of the 5-benzhydrylhydantoin, 8 g of the latter was heated with 30 g $Ba(OH)_2 \cdot 8H_2O$ and 150 ml water under a reflux condenser at 100° for an hour. Acidification with dilute hydrochloric acid brought down 8.45 g of a substance melting at 197-198° after recrystallization from aqueous alcohol. A mixed melting point determination with the acid prepared in the previous experiment did not give a depression; m.p. 185-186°.

0.0710 g substance: 6.1 ml N_2 (19°, 766 mm). 0.0919 g substance: 3.5 ml NaOH (F 0.9387). 0.0745 g substance. 0.0206 g Ag; 0.0821 g substance: 25.8 ml CH_4 (17°, 762.5 mm). Found %: N 9.90, E 279.7; % Ag 27.65; number of active hydrogen atoms 3.7 $C_{16}H_{15}O_3N_3$. Calculated %: N 9.85; E 284, number of active hydrogen atoms 4. $C_{16}H_{15}O_3N_2Ag$. Calculated %: Ag 27.62.

The analytical results show that alkaline hydrolysis of 5-benzhydrylhydantoin gave α-benzhydrylhydantoic acid. The anticipated α-amino acid was not formed either on acid or alkaline hydrolysis.

The transformations of α-benzhydrylhydantoic acid in acid and alkaline media were studied.

When boiled with 20% hydrochloric acid and with 20% sulfuric acid 2 g of the acid gave 1.7 g 5-benzhydrylhydantoin. Boiling of 1 g of the acid with concentrated hydrochloric acid gave 0.8 g of the hydantoin. When the acid was boiled with aqueous $Ba(OH)_2$ for 5 hours, it was quantitatively recovered unchanged.

Preparation of Mercaptophenylacetaldehyde by Rodionov's Method [18]

A reaction mixture comprising 40 g bromodiphenylacetaldehyde dissolved in 80 ml, 90% alcohol and a solution of 41 g sodium thiosulfate in 40 ml water was heated with stirring at the boil for 22 hours until the Beilstein reaction for chlorine was negative. During the reaction an oil settled out and sulfur was liberated. At the conclusion of the heating a stream of carbon dioxide was passed through the reaction flask, after which 60 ml 45% sulfuric acid was added; this caused a considerable volume of oily liquid to separate. The substance was extracted with ether and dried with sodium sulfate. After driving off the ether, the substance was distilled in high vacuum. In the first fractionation the substance boiled at 125-134°.

A second fractionation gave the following fractions: 1) to 120° a few drops; 2) 122° 10 g; 3) 123-132° 1.5 g; decomposition of the substance and separation of sulfur were observed.

The second fraction with an emerald-green color had a most unpleasant and very persistent odor. It gave positive reactions for sulfur and aldehyde group and was neutral to litmus. On standing in a closed vessel the color gradually changed from green to light-yellow. At the same time the reaction to litmus became acid. The substance did not give a color reaction with nascent nitrous acid and did not titrate with iodine, which indicated the absence of the SH group.

0.1649 g substance: 0.0150 g $BaSO_4$. 0.0909 g substance: 1.9 ml CH_4 (17°, 704.5 mm). 0.0926 g substance, 14.86 g benzene: Δt 0.155°. Found %: S 2.04; number of active hydrogen atoms 0.2090. M 206.3. $C_{14}H_{14}OS$. Calculated %: S 14.03; number of active hydrogen atoms 1. M 228.

The data showed that the substance that distilled over within a range of one degree is a mixture and not a pure compound.

Preparation of 2,4-dinitrophenylhydrazone of substance with b.p. 122° at a pressure of less than 1 mm. To a freshly prepared solution of 2,4-dinitrophenylhydrazine was added 0.5 g substance dissolved in alcohol. Almost at once a dark-red precipitate was formed, after a short time another 2,4-dinitrophenylhydrazone began to separate in the form

of yellow needles. On recrystallization from 90% alcohol, the dark-red 2,4-dinitrophenylhydrazone did not dissolve whereas the light-yellow hydrazone dissolved fairly quickly. The light-yellow substance melted at 145-146° and did not give a depression with an authentic sample of diphenylacetaldehyde 2,4-dinitrophenylhydrazone.

The dark-red 2,4-dinitrophenylhydrazone was recrystallized from ethylacetoacetate, m.p. 235-236°; a mixed test with benzophenone 2,4-dinitrophenylhydrazone did not give a depression. In view of the fact that the substance changed from neutral to acid on standing, it was oxidized with $KMnO_4$ solution. Oxidation of 3.6 g substance with b.p. 122° at a pressure of less than 1 mm consumed 2.28 g permanganate. The neutral product obtained was benzophenone (1.3 g). In the acid products of oxidation were found diphenylacetic acid (m.p. 144-145°) and a small admixture of benzoic acid; these were separated by fractional distillation. It follows that the substance with b.p. 122° in high vacuum consisted of benzophenone and a mixture of diphenylacetaldehyde and thiodiphenylacetaldehyde.

Preparation of the Mercaptoaldehyde by Reaction of Bromodiphenylacetaldehyde with NaSH

To 20 g bromodiphenylacetaldehyde dissolved in 50 ml dry benzene was added, in small portions, freshly prepared NaSH [20] suspended in benzene. During the addition heat was developed and the color became dark-blue. The end of the reaction was indicated by absence of heat development when fresh portions of NaSH were added and by a negative reaction for halogen. The benzene solution was decanted from the inorganic precipitate; the precipitate was washed with benzene and the wash liquor added to the main solution. After driving off the benzene, the substance was distilled in high vacuum to give 8 g blue liquid with b.p. 127-138° at a pressure below 1 mm. A second distillation at a pressure of less than 1 mm gave 2 fractions: 1) 123-133°, 3.45 g; 2) 134-138°, 1.25 g. Both fractions were blue, readily mobile liquids not giving a positive reaction for sulfur and with a neutral reaction to litmus. With 2,4-dinitrophenylhydrazine both fractions gave two 2,4-dinitrophenylhydrazones: benzophenone hydrazone (main product) and a small quantity of the hydrazone of diphenylacetaldehyde. Mixed tests with the authentic 2,4-dinitrophenylhydrazones gave no depression. The mass remaining after distillation gave a qualitative reaction for sulfur and the aldehyde group, but did not give a color reaction with nascent nitrous acid. Treatment with 2,4-dinitrophenylhydrazine gave a small amount of the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde.

Consequently the reaction with NaSH also failed to give mercaptophenylacetaldehyde, although the reaction was performed in very mild conditions: the reaction temperature did not rise above 30°. In the instant of its formation the mercaptophenylacetaldehyde is apparently decomposed into thiobenzophenone and formaldehyde, and the thiobenzophenone is oxidized to benzophenone by oxygen from the air. Furthermore, NaSH acted on bromodiphenylacetaldehyde as a reducing agent and reduced it to diphenylacetaldehyde, which was also detected in the reaction products.

SUMMARY

1. Preparations were carried out of 5-benzhydrylhydantoin (in 75% yield by Bucherer's method) and of α-benzhydrylhydantoic acid which had not previously been known. Their transformations in acid and alkaline media were studied.

2. Substitution of the halogen in bromodiphenylacetaldehyde by the mercapto group by the action of NaSH in an anhydrous medium was studied.

3. It was shown that the resultant mercaptodiphenylacetaldehyde is unstable and decomposes with formation of thiobenzophenone which undergoes oxidation to benzophenone. Moreover, NaSH acts on bromodiphenylacetaldehyde as a reducing agent and reduces it to diphenylacetaldehyde.

The reaction of bromodiphenylacetaldehyde with sodium thiosulfate by Rodionov's method proceeded in two directions: with formation of mercaptodiphenylacetaldehyde (which decomposed to thiobenzophenone which oxidized to benzophenone) and with formation of diphenylacetaldehyde and thiodiphenylacetaldehyde. The latter is also readily oxidized in the air.

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SYNTHESIS OF 2,3-DISUBSTITUTED QUINUCLIDINES

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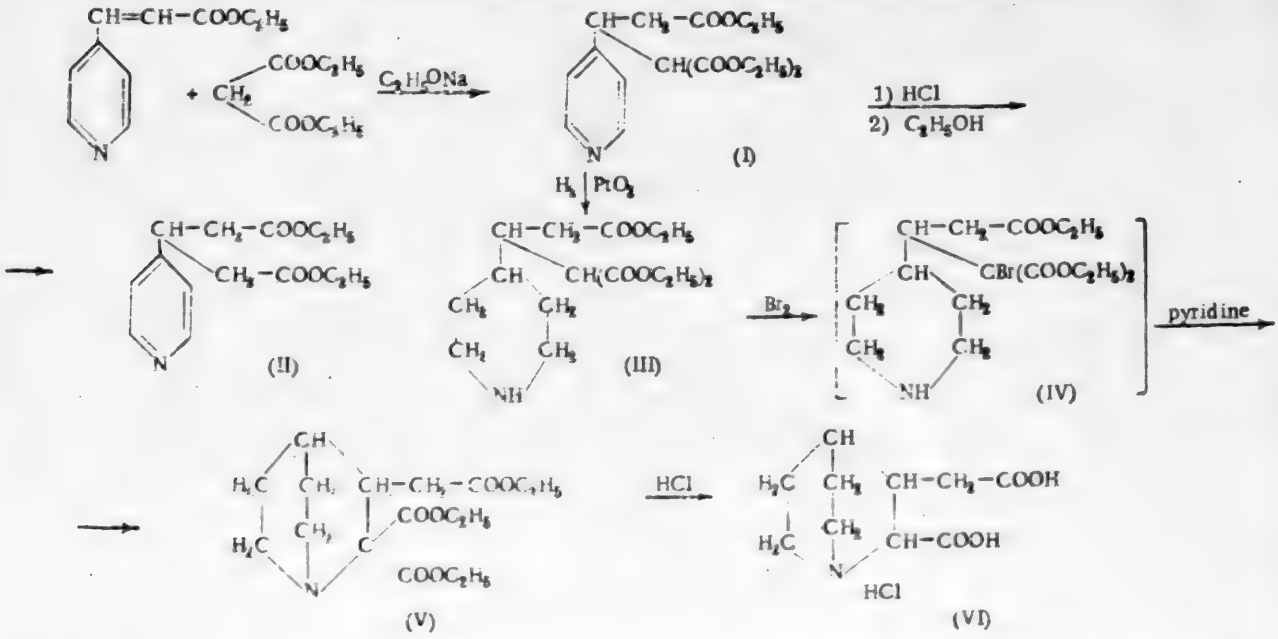
Substituted quinuclidines are of undoubted interest as a possible source of therapeutic substances. Up to recently, however, compounds of this series have not been subjected to extensive biological investigation due to the complexity of their preparation [1].

One of us, in collaboration with Dorokhova, recently developed a simple synthesis of 2-quinuclidinecarboxylic acid and its derivatives [2] and thus made possible a more extensive study of the biological and chemical properties of compounds of this class.

Continuing our work in this direction, we have realized the synthesis of [2-carboxyquinuclidyl-(3)]-acetic acid, some of its derivatives and products of their transformation, which are described in this paper.

2,3-Disubstituted quinuclidines have not been described in the literature; apart, therefore, from the possibility of investigating their biological properties, a study of the chemical properties of compounds of this series was also a matter of interest.

Our synthesis of [2-carboxyquinuclidyl-(3)]-acetic acid may be represented by the following scheme:



Preparation of the ethyl ester of β-dicarbethoxymethyl β-[pyridyl-(4)]-propionic acid (I), the starting material of the present synthesis was effected with the help of Michael's reaction. Ethyl malonate readily reacts with the equivalent amount of ethyl β-[pyridyl-(4)] acrylate in presence of sodium ethylate in alcoholic solution. The reaction is completed at room temperature in 5-6 hours or at 60° in one hour. (I) is formed in a yield of 94% of the theoretical. Substance (I) is a viscous liquid partly decomposing on distillation in vacuum. The latter operation is unnecessary because reaction product (I) is obtained in complete analytical purity in the conditions detailed in the experimental part.

Boiling of (I) with concentrated hydrochloric acid gives β-[pyridyl-(4)]-glutaric acid, which was identified in the form of its diethyl ester (II).

The hydrochloride of (I) is readily reduced to the corresponding piperidine derivative (III) in presence of Adams platinum catalyst at room temperature in alcoholic solution.

In the same conditions as for preparation of 2-quinuclidinecarboxylic acid [2], β-dicarbethoxymethyl-β-[piperidyl-(4)] propionic ester is then converted into the ethyl ester of β-dicarbethoxybromomethyl-β-[piperidyl-(4)]-propionic acid (IV) and then into the ethyl ester of [2,2-dicarbethoxyquinuclidyl-(3)]-acetic acid (V). The latter is transformed by prolonged digestion with concentrated hydrochloric acid into [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride (VI). The free acid is easily separated by treating the alcoholic solution of (VI) with the calculated amount of alcoholic solution of ammonia. The free acid is substantially insoluble in absolute alcohol, and it therefore separates by this treatment from sufficiently dilute solutions in the analytically pure form. Separation of the free acid from its hydrochloride via the silver salt was difficult to effect in practice because of the poor solubility of the silver salt in water.

The diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid may be prepared by reaction of the dichloroanhydride of the acid with alcohol or by two heatings of the hydrochloride of the acid with a 5% alcoholic solution of hydrogen chloride. In both cases the yield of diester is about 85%, but the second method gives a purer product.

The diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid is reduced with the help of lithium aluminum hydride with formation of 2-hydroxymethyl-3-(β-hydroxyethyl)-quinuclidine. The obtained glycol readily reacts with thionyl chloride to form 2-chloromethyl-3-(β-chloroethyl)-quinuclidine, a colorless, mobile liquid. This compound is transformed on standing into a spongy white mass, insoluble in ether. Polymeric products of the nature of quaternary salts are apparently formed. This process proceeds much more quickly with heating, thus, when pure 2-chloromethyl-3-(β-chloroethyl)-quinuclidine is distilled in vacuum, about 50% of it is converted into the polymer.

Heating of the hydrochloride of the dichloroanhydride of [2-carboxyquinuclidyl-(3)]-acetic acid with diethylaminoethanol gives the corresponding diester.

EXPERIMENTAL

Ethyl Ester of β-Dicarbethoxymethyl-β-[pyridyl-(4)]-propionic Acid (I). To an alcoholic solution of sodium ethylate prepared from 1.25 g sodium and 20 ml absolute alcohol is added 8.7 g ethyl malonate and 9.6 g β-[pyridyl-(4)] acrylic ester. The reaction mixture is energetically stirred until a homogeneous mass is formed, and then heated for an hour at 60°. The cooled solution is poured into 100 ml water containing 3.5 g acetic acid. The precipitated heavy oil is separated, the aqueous layer is exhaustively extracted with ether, the ether extract is mixed with the separated oil, washed with water until the ethereal solution is decolorized, and dried with sodium sulfate. After driving off the ether and removing its last traces in vacuum, the residue is a viscous oil, the ethyl ester of β-dicarbethoxymethyl-β-[pyridyl-(4)]-propionic acid. Weight 17.2 g. Yield 94.2% of the theoretical. B.p. 173-175° at 0.2 mm with partial decomposition. The compound dissolves readily in organic solvents, insoluble in water.

3.442 mg substance: 7.635 mg CO_2; 2.059 mg H_2O. 5.088 mg substance: 1.64 ml 0.01 N H_2SO_4. Found %: C 60.53, H 6.69, N 4.51. $C_{17}H_{23}O_6N$. Calculated %: C 60.55, H 6.82, N 4.15.

The hydrochloride is prepared by treating the compound with an alcoholic solution of hydrogen chloride until the reaction is acid to Congo. The resultant oil crystallizes on cooling. M.p. 121-122° (from alcohol-ether).

3.201 mg substance: 6.563 mg CO_2, 1.951 mg H_2O. 3.852 mg substance: 7.759 mg CO_2, 2.232 mg H_2O. 9.726 mg substance: 0.309 ml N_2 (22°, 749 mm). 9.456 mg substance: 0.302 ml N_2 (22°, 749 mm). Found %: C 54.92, 54.96, H 6.69, 6.51, N 3.02, 3.04. $C_{17}H_{23}O_6N \cdot HCl$. Calculated %: C 54.63, H 6.43, N 3.75.

Ethyl Ester of β-[Pyridyl(4)]-glutaric Acid (II). 4.4 g ethyl ester of β-dicarbethoxymethyl-β-[pyridyl(4)]-propionic acid and 44 ml concentrated hydrochloric acid are boiled for 8 hours. The solution is then filtered to free it from turbidity and evaporated in vacuum, the residual oil is dried by adding alcohol and distilling it off (this process is repeated two more times). To the resultant hydrochloride of β-[pyridyl-(4)]-glutaric acid is added 35 ml 5% alcoholic solution of hydrogen chloride, and the reaction mass is heated at the boil for 3 hours. The alcohol is driven off in vacuum, the residue is treated with 50% potassium carbonate solution and extracted with ether. The ethereal solution is dried with potassium carbonate. After driving off the ether, the substance is distilled in vacuum. B.p. 146-148° at 0.2 mm. Yield 2.92 g or 84.4% of the theoretical. Colorless viscous liquid, soluble in organic solvents, insoluble in water.

4.430 mg substance: 10.270 mg CO_2, 2.902 mg H_2O. 4.978 mg substance: 1.87 ml 0.01 N H_2SO_4. Found %: C 63.27, H 7.33, N 5.25. $C_{14}H_{19}O_4N$. Calculated %: C 63.40, H 7.17, N 5.28.

Ethyl Ester of β-Dicarbethoxymethyl-β-[piperidyl-(4)]-propionic Acid (III). A solution of 47.8 g ethyl β-dicarbethoxymethyl-β-[pyridyl-(4)]-propionate hydrochloride in 330 ml absolute alcohol is reduced at room temperature in presence of 1 g platinum oxide. After absorption of the theoretical amount of hydrogen (40-45 hours) the catalyst is filtered off and the filtrate evaporated in vacuum. The residual caramel-like mass is the hydrochloride of ethyl β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionate. Yield quantitative.

The base which separates on treatment of the hydrochloride with 50% potassium carbonate solution changes into an undistillable foamy mass when heated in vacuum, apparently a lactam. The reduction product was characterized by preparation of the ethyl ester of β-dicarbethoxymethyl-β-[N-acetylpiperidyl-(4)]-propionic acid. Acetylation is effected in the following manner. Ethyl β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionate and 5 times the amount of acetic anhydride are heated 1 hour on a boiling water bath. The acetic anhydride is distilled off, the residue dissolved in ether, the ether solution washed with aqueous sodium bicarbonate and dried with potassium carbonate. After removal of the ether, the residue is distilled in vacuum. B.p. 206-207° at 0.3 mm. Viscous liquid with a greenish tint, readily soluble in organic solvents, insoluble in water.

7.634 mg substance: 16.595 mg CO_2, 5.501 mg H_2O. 17.000 mg substance: 0.573 ml N_2 (25°, 726 mm). Found %: C 59.32; H 8.06, N 3.69. $C_{19}H_{31}O_7N$. Calculated %: C 59.22; H 8.05; N 3.64.

Ethyl [2,2-Dicarbethoxyquinuclidyl-(3)]-acetate (V). The hydrochloride of β-dicarbethoxymethyl-β-[piperidyl-(4)]-propionic ester prepared by reduction of 47.8 g of the corresponding pyridine derivative is dissolved in 150 ml dry chloroform. To the solution is added a solution of 20.4 g bromine in 154 ml chloroform at room temperature with good stirring over a period of 8 hours. The reaction mass is allowed to stand for another 12-14 hours; during this period the solution is completely decolorized; the chloroform is then removed in vacuum. The residue is dissolved in 140 ml water, the same volume of 50% potassium carbonate solution is added, and the separated oil is extracted with ether. Without drying, the ethereal solution of β-dicarbethoxybromomethyl-β-[piperidyl-(4)]-propionic ester is evaporated in vacuum. The residual oil is digested for 2 hours with 390 ml pyridine; the reaction mass acquires a dark-brown color. The pyridine is distilled off; the residual dark-brown, viscous oil is well stirred with 50% potassium carbonate solution and extracted with ether. The ethereal solution is dried with potassium carbonate, the ether is driven off, and the residue distilled in vacuum. Yield 31.45 g ethyl ester of [2,2-dicarbethoxyquinuclidyl-(3)-acetic acid with b.p. 147-148° at 0.25 mm. A colorless, mobile liquid, readily soluble in water and organic solvents. The yield is 72% of the theoretical.

d_4^{22} 1.134; n_D^{18} 1.4793; MR_D 85.30. $C_{17}H_{27}O_6N$. Calculated: MR_D 85.20.

Methiodide of ethyl [2,2-dicarbethoxyquinuclidyl-(3)]-acetate, white, lustrous platelets, readily soluble in water and alcohol, insoluble in ether. M.p. 139-141° (from alcohol-ether).

5.424 mg substance: 6.75 ml 0.02 N $Na_2S_2O_3$. 6.399 mg substance: 1.28 ml 0.01 N H_2SO_4. 8.378 mg substance: 1.57 ml 0.01 N H_2SO_4. Found %: I 26.33, N 2.86, 2.62. $C_{18}H_{30}O_6NI$. Calculated %: I 26.29; N 2.90.

Hydrochloride of [2-Carboxyquinuclidyl-(3)]-acetic Acid (VI). 27.5 g ethyl [2,2-dicarbethoxyquinuclidyl-(3)-acetate and 270 ml concentrated hydrochloric acid are heated at the boil for 16 hours. The hydrochloric acid solution is then decolorized with carbon and evaporated on the water bath until crystallization begins. The lustrous, white needles of the hydrochloride of [2-carboxyquinuclidyl-(3)]-acetic acid come down on cooling and are carefully drained at the pump and washed with acetone. The filtrate is concentrated in vacuum to a slurry, diluted with acetone, filtered, and washed with acetone. A further amount of hydrochloride is thus separated and is added to the main crop. Total yield 18.4 g or 91.6% of the theoretical. White crystals, readily soluble in water, poorly soluble in hot alcohol, insoluble in cold alcohol, acetone, and ether. M.p. 253-254° (with decomposition).

For analysis, part of the substance is dissolved in hot absolute alcohol and reprecipitated from solution with cold ether. M.p. 254-255° (with decomposition).

3.010 mg substance: 5.417 mg CO_2, 1.822 mg H_2O. 3.068 mg substance: 5.405 mg CO_2; 1.839 mg H_2O. 4.401 mg substance: 2.574 mg AgCl. 5.330 mg substance: 3.138 mg AgCl. Found %: C 48.31, 48.08, H 6.66, 6.70; Cl 14.48, 14.54. $C_{10}H_{15}O_4N \cdot HCl$. Calculated %: C 48.10; H 6.42; Cl 14.62.

[2-Carboxyquinuclidyl-(3)]-acetic Acid. a) 6.4 g [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride, 1.1 g silver oxide and 6 ml water are shaken for 2 hours. The mass is diluted with 40 ml water, brought to the boil, filtered and washed with 45 ml hot water. The filtrate is saturated with hydrogen sulfide, the precipitated silver sulfide is filtered off, the colorless aqueous solution of [2-carboxyquinuclidyl-(3)]-acetic acid is evaporated to dryness in a vacuum. Yield 0.15 g acid with m.p. 265-267°. White crystals, readily soluble in water and dilute mineral acids, insoluble in organic solvents. Yield is 43.8% of theoretical.

b) 3.5 g of [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride is dissolved at the boil in 250 ml absolute alcohol. The alcoholic solution is filtered from turbidity and treated with 4.3 ml 6.5% alcholic solution of ammonia. On standing for 48 hours, 2.02 g [2-carboxyquinuclidyl-(3)]-acetic acid comes down in the form of white plates. M.p. 273°, yield 87.0% of the theoretical.

4.409 mg substance: 9.147 mg CO_2, 2.771 mg H_2O. 4.491 mg substance: 9.312 mg CO_2; 2.892 mg H_2O. 6.744 mg substance: 0.402 ml N_2 (18°, 732 mm). 6.709 mg substance: 0.384 ml N_2 (18°, 732 mm). Found %: C 56.61, 56.59; H 6 91, 7.21; N 6.74, 6.47. $C_{18}H_{15}O_4N$. Calculated %: C 56.34; H 7.04; N 6.57.

Diethyl Ester of [2-Carboxyquinuclidyl-(3)] acetic Acid.

a) 7 g [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride and 100 ml purified thionyl chloride are heated on a water bath at 70° for 10 hours. The resultant hydrochloride of the dichloroanhydride of [2-carboxyquinuclidyl-(3)]-acetic acid is insoluble in thionyl chloride. The excess of thionyl chloride is distilled off in vacuum. Its complete removal is effected by twice adding absolute benzene and distilling in vacuum. Into the hydrochloride of the dichloroanhydride is run 140 ml absolute alcohol. The alcoholic solution is heated at the boil for 3 hours, and then the alcohol is driven off in vacuum, the residue treated with 50% potassium carbonate solution, and the separated oil extracted with ether. The ethereal solution is dried with potassium carbonate, then the ether is driven off and the residue distilled in vacuum. 6 25 g diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid is obtained with b.p. 126° at 0.3 mm. Yield 82 7% of the theoretical. The compound is a yellow, mobile liquid whose color is not eliminated by repeated distillations. Readily soluble in water and organic solvents; n_D^{18} 1.4797.

6 970 mg substance 15.949 mg CO_2; 5.281 mg H_2O. 4 400 mg substance :10.063 mg CO_2; 3.318 mg H_2O. 4.309 mg substance: 1.63 ml 0.01 N H_2SO_4. Found %: C 62.44, 62.41, H 8.47, 8.44; N 5 30. $C_{14}H_{23}O_4N$

b) The diethyl ester of [2-carboxyquinuclidyl-(3)] acetic acid may be obtained in the form of a colorless liquid by the following method. 15 g [2-carboxyquinuclidyl-(3)]-acetic acid hydrochloride and 150 ml 5% alcoholic solution of hydrogen chloride are heated at the boil until solution is complete (this requires about 6 hours) The alcohol is driven off in vacuum; a fresh addition of 150 ml 5% alcoholic solution is made and heating continued for 4 hours. After removal of the alcohol, the reaction mass is worked up as in a) Vacuum distillation gives the diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid in the form of a colorless mobile liquid with b p 125° at 0.3 mm, n_D^{18} 1.4797.

Methiodide of the diethyl ester of [2-carboxyquinuclidyl-(3)] acetic acid white, lustrous needles, readily soluble in water and alcohol, insoluble in ether and acetone. M.p. 140-141° (from a mixture of alcohol and ether).

10 666 mg substance. 0 333 ml N_2 (22 5°, 716 mm). 10 298 mg substance: 0 303 ml N_2 (22.5°, 716 mm) 0 1173 g substance 0 0661 g AgI. Found %: N 3.39, 3 20. I 30 47. $C_{15}H_{26}O_4NI$. Calculated %: N 3.40; I 30.90

2 Hydroxymethyl 3-(β hydroxyethyl) quinuclidine.

A solution of 8 2 g diethyl ester of [2-carboxyquinuclidyl-(3)]-acetic acid in 82 ml absolute ether is added with stirring to a suspension of 4.64 g lithium aluminum hydride in 92 ml ether over a period of 15 minutes, and the reaction mass is heated at the boil for an hour. Addition is then made, while cooling, of 9 ml water the precipitated lithium and aluminum hydroxides are drained at the pump and thoroughly washed on the filter with chloroform. The combined ethereal and chloroform filtrates are dried with potassium carbonate Removal of the chloroform and ether leaves 5 g 2-hydroxymethyl 3 (β hydroxyethyl)-quinuclidine. Yield 88 7% of the theoretical. Colorless extremely viscous oil, b p 156-157° at 0.4 mm Readily soluble in water and organic solvents

9 327 mg substance: 0 637 ml N_2 (21°, 718 mm) 5 225 mg substance: 0.353 ml N_2 (18 5°, 728mm) Found %: N 7 49, 7 58 $C_{10}H_{19}O_2N$ Calculated %: N 7 57

The hydrochloride is obtained by treating an ethereal solution of the compound with an alcoholic solution of hydrogen chloride until the reaction is acid to Congo. White, hygroscopic crystals readily soluble in water and alcohol, insoluble in ether or chloroform.

2-Chloromethyl-3 (β-chloroethyl)-quinuclidine

To 5 22 g 2-hydroxymethyl-3 (β-hydroxyethyl)-quinuclidine hydrochloride suspended in 20 ml dry chloroform is gradually added 18 ml thionyl chloride while cooling. The homogenous solution is heated at the boil for 30 minutes The chloroform and excess thionyl chloride are driven off in vacuum and the last traces of thionyl chloride are eliminated by three times adding and distilling off benzene in vacuum. 5.72 g 2-chloromethyl 3-(β-chloroethyl)-quinuclidine hydrochloride is obtained Yield 94% of the theoretical White hygroscopic crystals with m.p. 139-140°.

The base is obtained by treating the hydrochloride with 50% potassium carbonate solution and extracting with chloroform. The chloroform extract is dried with potassium carbonate, the chloroform is driven off and the residue distilled in vacuum. B p. 120-122° at 0.25 mm Colorless mobile liquid, readily soluble in water and organic solvents.

11.106 mg substance: 4.76 ml 0.01 N H_2SO_4. 4.619 mg substance: 1.73 ml 0.01 N H_2SO_4.
Found %: N 6.00, 6.04; $C_{13}H_{21}NCl_2$. Calculated %: N 6.31.

Methiodide of 2-chloromethyl-3-(β-chloroethyl)-quinuclidine is prepared by running the equivalent amount of methyl iodide into an ethereal solution of the compound. White crystals, readily soluble in water and alcohol, insoluble in ether. M.p. 136°.

12.600 mg substance: 0.421 ml N_2 (20°, 736 mm). 13.700 mg substance: 0.436 ml N_2 (20°, 736 mm).
6.030 mg substance: 10.03 ml 0.01 N $Na_2S_2O_3$. 5.971 mg substance: 9.94 ml 0.01 N $Na_2S_2O_3$.
Found %: N 3.77, 3.81; I 35.20, 35.22. $C_{14}H_{24}NCl_2I$. Calculated%: N 3.84; I 34.90.

Di (diethylaminoethyl) Ester of [2-Carboxyquinuclidyl-(3)] acetic Acid.

40 ml diethylaminoethanol and the hydrochloride of the dichloroanhydride of [2-carboxyquinuclidyl-(3)] acetic acid prepared from 3 g of the acid hydrochloride are heated on a water bath at 80-85° for 3½ hours. The excess diethylaminoethanol is then distilled off in vacuum, the residue is treated with 50% potassium carbonate, the separated brown oil is extracted with chloroform. Following the removal of the chloroform, the ester is distilled in vacuum. B.p. 187-189° at 0.3 mm. After a second distillation the substance is obtained in the form of a yellow, mobile liquid, readily soluble in water and organic solvents. Yield 3.42 g or 62% of the theoretical.

3.700 mg substance: 8.661 mg CO_2; 3.282 mg H_2O. 5.529 mg substance: 12.977 mg CO_2; 5.031 mg H_2O.
6.915 mg substance: 5.04 ml 0.01 N H_2SO_4. Found %: C 63.88, 64.05; H 9.92, 10.18; N 10.20. $C_{22}H_{41}O_4N_3$.
Calculated %: C 64.23; H 9.98; N 10.22.

Trimethiodide of di (diethylaminoethyl) ester of [2-carboxy-quinuclidyl-(3)] acetic acid is prepared by mixing an alcoholic solution of the compound with methyl iodide. M.p. 197-199° (with decomposition). White crystals, very soluble in water, insoluble in alcohol, ether or acetone.

6.880 mg substance: 2.44 ml 0.01 N H_2SO_4. Found %: N 4.97. $C_{25}H_{53}O_4N_3I_3$. Calculated %: N 5.02.

SUMMARY

1. A method is developed for preparing 2,3 disubstituted quinuclidines starting from the ethyl ester of β-[pyridyl-(4)]-acrylic acid.

2. [2-Carboxyquinuclidyl-(3)] acetic acid and some of its derivatives and transformation products are synthesized.

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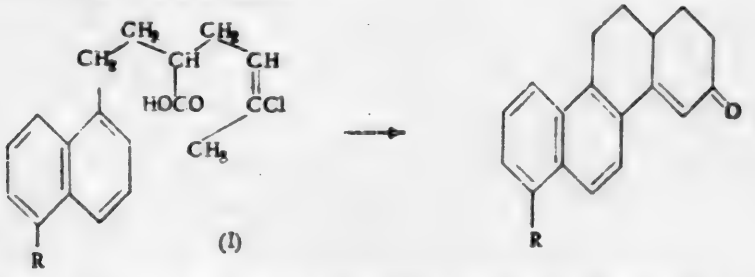
* See Consultants Bureau English translation, page 731.

SYNTHESIS OF POLYNUCLEAR HYDROAROMATIC KETONES

VI. 3 KETO-1,2,3,11,12,12a-HEXAHYDRO-6,7-ACECHRYSENE

S. A. Vardanyan, P. A. Zagorets and G. T. Tatevosyan

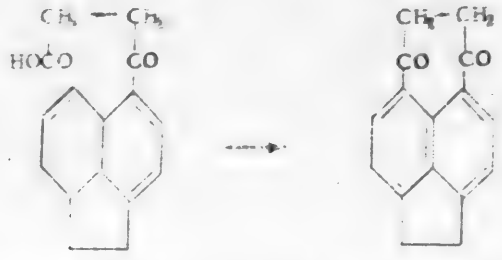
In Communication III [1] it was shown that α-(3 chloroacetyl)-γ-(1-naphthyl)-butyric acid (I, R = H) is hydrolized by sulfuric acid at the chlorine atom and the resultant keto acid undergoes a double consecutive cyclization into a ketone of the chrysene series:



(I)

The presence of a methoxyl group in the 5-position of the naphthalene nucleus (I, R = CH_3O) which, according to the literature [2] promotes peri cyclization of the corresponding γ-(1-naphthyl)-butyric acid, does not in this case hinder the formation of a ketone of the chrysene series [3]; this is evidently due to the presence of a substituent (in the present case the γ chloroacetyl radical) in the α-position to the carboxyl group which favors the usual ortho-cyclization of γ-(1-naphthyl)-butyric acids [4].

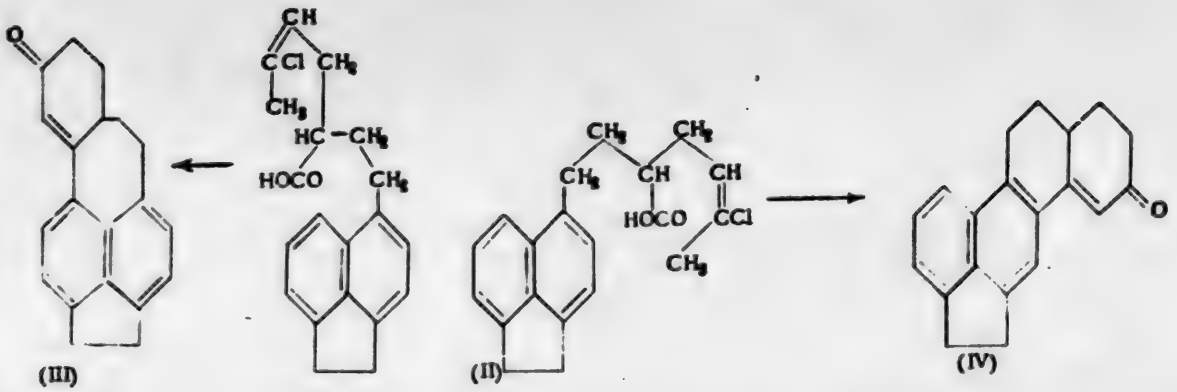
A case of peri-cyclization was described by Fieser and Peters [5] who cyclized β-(3-acenaphthoyl)-propionic acid by fusion with a mixture of aluminium chloride and sodium chloride. The product of cyclization was diketo-dihydro-homophenalene



whose structure was demonstrated by oxidation to naphthalene 1,4,5,8-tetracarboxylic acid. The authors explain the formation of a product of peri-cyclization by the presence in the side chain of a carbonyl group which hinders ortho-cyclization, and by the para-directive influence of the ace bridge in the nucleus.

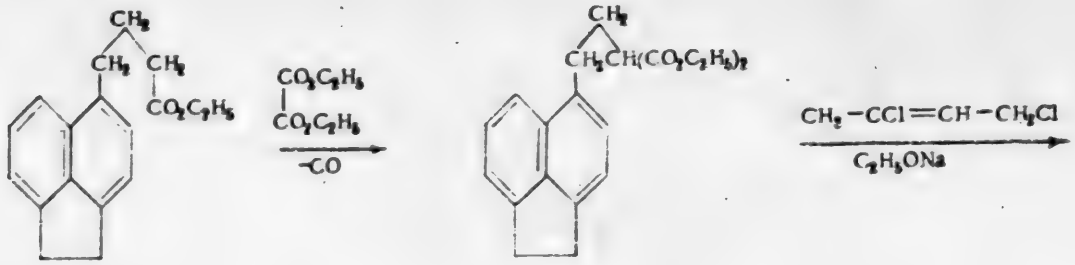
In view of the above considerations it could be assumed that the effect of sulfuric hydrolysis and cyclization of α-(3-chloroacetyl)-γ-(3-acenaphthyl)-butyric acid (II) would be the formation, in place of 3-keto-1,2,3,11,12,12a-hexahydro-6,7-acechrysene (IV) or side by side with it, of the isomeric ketone (III) with one seven-membered ring: (See top of next page).

The present communication is devoted to the synthesis of acid (III) and the study of the product of its interaction with sulfuric acid.

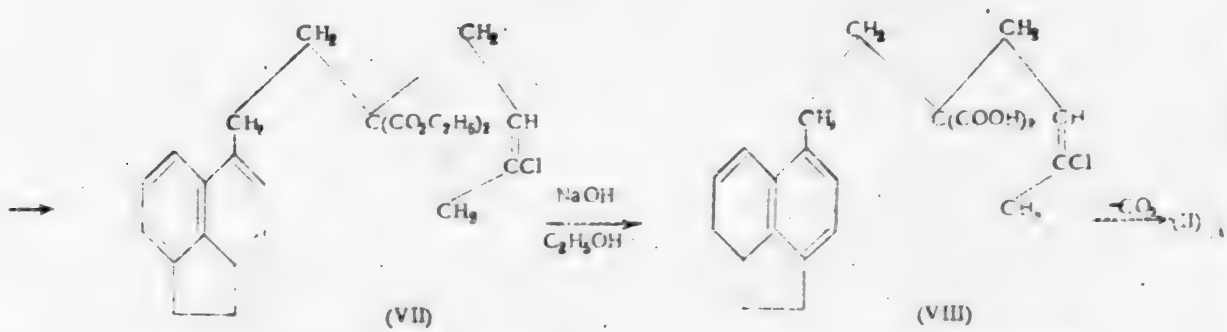


(III) (II) (IV)

Acid (II) was synthesized from the ethyl ester of γ-(3-acenaphthyl)-butyric acid previously described by Fieser and Peters [5].



(V) (VI)

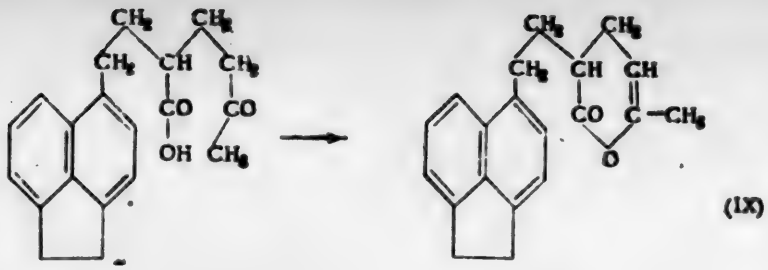


(VII) (VIII)

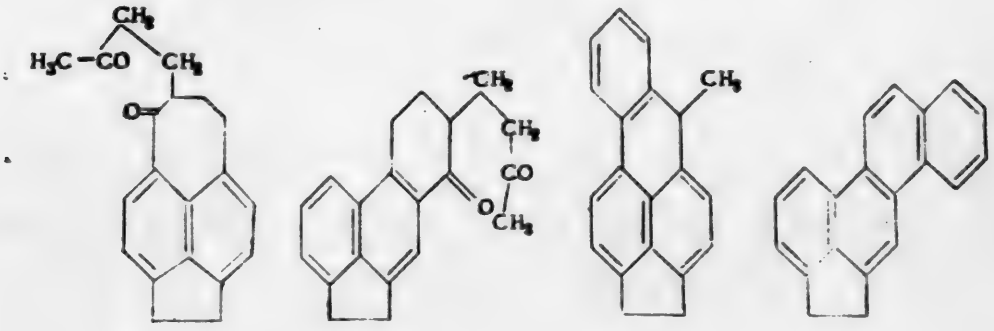
The product of reaction of acid (II) with sulfuric acid (s.g. 1.76) at 50-55° had the composition $C_{19}H_{16}O_2$ and not the composition of the anticipated pentacyclic ketone (III or IV) $C_{19}H_{14}O$. A substance with composition $C_{19}H_{16}O_2$ could be the unsaturated lactone (IX) which could be formed from the product of sulfuric acid hydrolysis (the keto acid) by lactonization followed by dehydration of the lactone: (See top of next page) or it could be one of the diketones (X) and (XI) which could be formed from the same keto acid by intramolecular acylation in the peri- or ortho-position respectively (See next page).

The nature of the compound was elucidated by treating it with boiling aqueous alkali. A salt was not formed as was to be expected in presence of a lactone, but an intramolecular aldol condensation took place with formation of a pentacyclic ketone with the composition $C_{19}H_{12}O$.

Consequently, contrary to the previously studied cases of sulfuric acid hydrolysis and twofold cyclization of α (3-chlorocrotyl) γ arylbutyric acids, in this case the transformations initiated by sulfuric acid stopped at the stage of formation of the tetracyclic diketone.



(IX)



(X) (XI) (XII) (XIII)

In Fig. 1 the ultraviolet absorption curve of ketone $C_{18}H_{18}O$ is compared with the absorption curve of 3-keto-1,2,3,11,12,12a-hexahydrochrysene which was plotted by Wilds and co-workers [6].

The close similarity between the curves is evidence that the investigated ketone is also an α,β-unsaturated ketone with the conjugated double bond system of 1-naphthalacetone (bifurcated maximum at 275-280 $m\mu$), containing the cyclic system of chrysene. The latter fact was confirmed also by study of the product of dehydrogenation of the ketone.

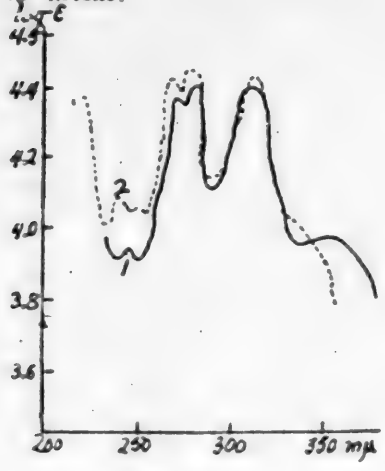


Fig. 1.

1 - Absorption curve of ketone $C_{18}H_{18}O$;

2 - absorption curve of 3-keto-1,2,3,11, 12, 12a-hexahydrochrysene.

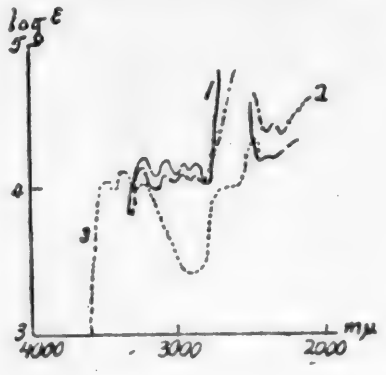


Fig. 2.

1 - Absorption curve of hydrocarbon $C_{19}H_{14}$;

2 - absorption curve of 3-methylchrysene;

3 - absorption curve of benzanthrene.

If the structure of the ketone were to be represented by formula (III), then its dehydrogenation ought to lead to isomerization of the seven-membered ring into a six-membered ring with formation of methyl-acebenzanthrene (XII), another possibility would be complete cleavage of the methyl group with formation of acebenzanthrene. But if the ketone has structure (IV), the product of its dehydrogenation should be 6,7-acechrysene (XIII).

In Figure 2 the absorption curve of the product of dehydrogenation melting at 238-239° and corresponding in composition to formulas (XII) and (XIII) is compared with the absorption curve of 3-methylchrysene, prepared by the action of methyl magnesium iodide on 3-keto-1,2,3,11,12,12a-hydrochrysene followed by dehydrogenation of the product formed. The complete similarity between the curves of both hydrocarbons and their similarity to the absorption curve of chrysene [7], as well as the coincidence of their maxima (318-322, 306-310, 294-296, 283-287 $m\mu$), confirm that these hydrocarbons contain an identical system of condensed aromatic nuclei. Moreover, these curves both in

general form and in the position of the maxima differ sharply in an identical manner from the absorption curve of benzanthrene [8] which is plotted in the same diagram.

Consequently, the absorption curves of the investigated compounds in conjunction with the method of preparation and the analytical data demonstrate that the hydrocarbon is 6,7-acechrysene (XIII), while the ketone whose dehydrogenation yields this hydrocarbon is 3-keto-1,2,3,11,12,12a-hexahydro-6,7-acechrysene (IV).

EXPERIMENTAL

The starting β-(3-acenaphthoyl)-propionic acid was prepared as described by Fieser and Peters [5] by condensing succinic anhyuride with acenaphthene in presence of aluminum chloride in nitrobenzene solution. The acid was purified from the isomeric β-(1-acenaphthoyl)-propionic acid via the sparingly soluble sodium salt and twice recrystallized. It then melted at 208°. Reduction of 50 g of the keto acid with zinc amalgam and hydrochloric acid according to the general procedure of Martin [9], gave 30.8 g (65.2% of the theoretical amount) of γ-(3-acenaphthyl)-butyric acid with m.p. 142-143°.

Ethyl ester of γ-(3-acenaphthyl)-butyric acid (V). A mixture of 100 g γ-(3-acenaphthyl)-butyric acid, 500 ml 96% alcohol and 25 ml concentrated sulfuric acid was boiled on the water bath for 6 hours, following which about 200 ml alcohol was driven off and the cooled mixture diluted with 500 ml water. The product was extracted with ether, the ethereal solution was washed with dilute sodium carbonate solution and then with water and dried with anhydrous sodium sulfate. After driving off the ether, distillation of the product in vacuum gave 101.5 g (90.9% of the theoretical) viscous liquid with b.p. 200-202° at 3 mm. The distilled material completely crystallized on standing. M.p. 39°. The ethyl ester of γ-(3-acenaphthyl)-butyric acid was described by Fieser and coworkers [10] as a viscous liquid with b.p. 188° at 0.5 mm.

β-(3-Acenaphthyl)-ethylmalonic ester (VI). To 6.1 g sodium, pulverized in boiling toluene and freed from toluene by washing with dry ether, was added 150 ml absolute ether, followed dropwise by a solution of 12.6 g absolute alcohol in 50 ml dry ether. At the conclusion of the violent reaction, the mixture was boiled on the water bath for 3 hours. To the cooled suspension of alcoholate was then gradually added a solution of 57 g ethyl oxalate in 50 ml absolute ether. Within 30 minutes of the termination of the violent reaction, addition was made to the reaction mixture of a solution of 70 g ester (V) in 100 ml absolute ether. The mixture was gently boiled on the water bath for 20 hours and after cooling it was decomposed by gradual addition of sulfuric acid (15 g conc. acid in 200 ml water). The product was extracted with ether and the ethereal solution was twice washed with water and dried with sodium sulfate. After the ether had been driven off, the product was decomposed by heating in a vacuum of the order of 8-10 mm until the frothing due to evolution of carbon monoxide had ceased. Two distillations in vacuum gave 69 g (67.5% of the theoretical yield) of the monosubstituted malonic ester (VI) in the form of a viscous liquid with b.p. 216-218° at 3 mm.

0.1021 g substance: 0.2776 g CO_2, 0.0668 g H_2O. 0.1102 g substance: 0.3004 g CO_2, 0.0714 g H_2O. Found %: C 74.15, 74.34; H 7.20, 7.19. $C_{21}H_{24}O_4$. Calculated %: C 74.12; H 7.06.

[β-(3-Acenaphthyl)-ethyl-(3-chloro)-crotyl]-malonic ester (VII). To a solution of sodium alcoholate prepared from 11.5 g sodium and 100 g absolute alcohol was added 170 g monosubstituted malonic ester (VI). After 30 minutes' standing, 75 g freshly distilled 1,3-dichlorobutene-2 was gradually run in with stirring. The reaction mixture was boiled for 6 hours, after which water acidified with hydrochloric acid was added. The reaction product was dissolved in ether, the ethereal solution was washed with water and dried over sodium sulfate. The solvent was driven off and the residue distilled twice in vacuum to give 102 g (47.6% of the theoretical amount) of the disubstituted malonic ester (VII) in the form of a viscous liquid with b.p. 230-232° at 3 mm. It crystallized completely after standing for two days. M.p. 46-47° after recrystallization from alcohol.

0.1194 g substance: 0.0406 g AgCl. 0.1188 g substance: 0.0398 g AgCl. Found %: Cl 8.41, 8.29. $C_{25}H_{29}O_4Cl$. Calculated %: Cl 8.28.

[β-(3-Acenaphthyl)-ethyl-(3-chloro)-crotyl]-malonic acid (VIII). A mixture of 112 g of the disubstituted malonic ester (VII), 21 g NaOH and 550 ml 90% alcohol was refluxed for 6 hours; 300 ml water was then added and the alcohol distilled off completely. After cooling, the alkaline solution was washed with ether and gently heated on the water bath for complete removal of the ether. Acidification of the cooled solution with dilute hydrochloric acid caused separation of a crystalline substance which melted at 174-175° after recrystallization from benzene. Yield 92.7 g (95.2% of the theoretical amount).

0.1094 g substance: 0 0412 g AgCl. 0.1140 g substance: 0.0430 g AgCl. Found %: Cl 9.34, 9.39. $C_{22}H_{21}O_4Cl$. Calculated %: Cl 9.53.

α-(3-Chlorocrotyl)-γ-(3-acenaphthyl)-butyric acid (II). 90.7 g of the disubstituted malonic acid (VIII) was decarboxylated by heating under reduced pressure. The resultant oil solidified when triturated with methyl alcohol. Recrystallization from alcohol gave 60 g (75% of the theoretical amount) of a colorless crystalline substance with m.p. 114-115°.

0.1024 g substance: 0.0431 g AgCl. 0.1026 g substance: 0.0439 g AgCl. Found %: Cl 10.41, 10.59. $C_{18}H_{21}O_2Cl$. Calculated %: Cl 10.80.

1-Keto-2-(γ-ketobutyl)-1,2,3,4-tetrahydro-8,9-acephenanthrene (XI). To 75 g sulfuric acid (s.g. 1.76) was gradually added 10 g of the pulverized substituted butyric acid (II) with stirring. After standing for half an hour, the mixture was heated on a water bath in a carbon dioxide current at 50-55° for 35-40 minutes until acid (II) had dissolved completely. The mass was then left at room temperature for 3 hours, after which period it was poured on to ice. The separated product was dissolved in ether, the ethereal solution washed with dilute caustic alkali, then with water, and dried with sodium sulfate. Removal of the ether left 4.3 g yellow crystals (48.4 % of the theoretical amount on the basis of the formula $C_{18}H_{18}O_2$). M.p. 115-116° after recrystallization from methyl alcohol.

0.0926 g substance 0 2797 g CO_2. 0.0592 g H_2O. 0.0992 g substance: 0.2980 g CO_2, 0.0612 g H_2O. Found %: C 82.37, 81 92; H 7.10, 6.88. $C_{18}H_{18}O_2$. Calculated %: C 82.19; H 6.85.

In more drastic conditions of treatment with sulfuric acid (higher concentration and temperature and more prolonged heating), the starting substance was almost completely sulfonated.

3-Keto-1,2,3,11,12,12a-hexahydro-6,7-acechrysene (IV). 3 g diketone (XI) was boiled for 4 hours with 40 ml 20% NaOH solution. The substance at first melted, then changed into a solid clot and finally disintegrated into powder. This was filtered, washed with water and twice recrystallized from methyl alcohol (boiling with animal charcoal). Yield 1.9 g (67.6% of the theoretical) of light-yellow, lustrous leaflets with m.p. 184-185°.

0.1012 g substance: 0.3240 g CO_2; 0.0610 g H_2O. Found %: C 87.31; H 6.69. $C_{18}H_{16}O$. Calculated %: C 87.69; H 6 58.

The 2,4-dinitrophenylhydrazone, prepared in an alcoholic medium and recrystallized from chloroform-alcohol mixture, had m.p. 171-172°.

0.1076 g substance 12.8 ml N_2 (19.5° 675 mm). Found %: N 12.33. $C_{24}H_{22}O_4N_4$. Calculated %: N 12 33.

6,7-Acechrysene (XIII). 2.5 g ketone (IV) was dehydrogenated with 0.5 g palladized carbon (10% Pd). Dehydrogenation was performed in a gentle stream of CO_2 at 280-300° for 4 hours. The dehydrogenation product was extracted with benzene. Attempts to purify the crude dehydrogenizate (after removal of the benzene) by sublimation were unsuccessful because it decomposed at atmospheric pressure without subliming. It was purified by 3 recrystallizations from benzene-alcohol mixture (boiling with charcoal). Yield 0.5 g crystals with a faint yellow tint, m.p. 238-239°.

0.0906 g substance 0 3124 g CO_2, 0 0400 g H_2O. Found % C 94.04 H 5.71 $C_{18}H_{14}$. Calculated %: C 94.44; H 5.56.

3-Methylchrysene was prepared by the method of Wilds and Shunk [11] by the action of magnesium methyl iodide on 3-keto 1 2 3 11 12 12a hexahydrochrysene [1] followed by dehydrogenation of the unpurified product (m.p. 75-90°) with palladized carbon. Two recrystallizations from benzene-alcohol mixture gave colorless crystals with m.p. 172° (Wilds and Shunk report m.p. 172.5-173.5°).

The orange picrate melted at 165° (the same authors give 166.5-167.5°).

SUMMARY

1. α-(3-Chlorocrotyl)-γ-(3-acenaphthyl)-butyric acid was synthesized and the product of sulfuric acid hydrolysis and cyclization of this acid was investigated.

2. It was shown that, in spite of the presence in the naphthalene nucleus of the starting acid of the 4,5-ace-bridge which favors peri-cyclization of γ-(1-naphthyl)-butyric acids, in the present case ortho-cyclization took place, leading to formation of a compound with the cyclic system of chrysene

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* See Consultants Bureau English translation, page 293, ff.

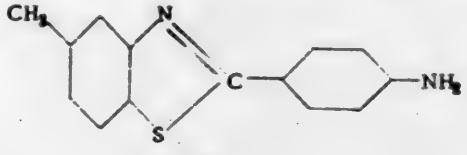
** See Consultants Bureau English translation, page 1349 ff.

IMIDAZOLE DERIVATIVES

VI. SYNTHESIS OF SOME POLYBENZIMIDAZOLES [1]

B. A. Porai-Koshits, L. S. Efros and E. S. Boichinova

It has been known for a long time that the yellow primuline dyes formed by treatment of p-toluidine with sulfur contain as their main grouping 2-p-aminophenyl-5-methylbenzothiazole (I) (dehydrothio-p-toluidine) and products of its further condensation with sulfur and p-toluidine containing two or even three benzothiazole residues.

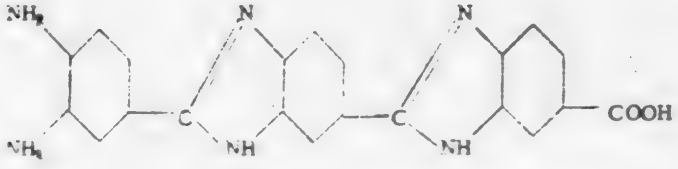


(I)

The thiazole ring [4] is considered to be the chromophoric group of these dyes.

Analogous compounds containing imidazole rings have not hitherto been obtained, and we have therefore undertaken the synthesis of these previously unknown compounds by our previously developed method [5] of condensation of o-diamines with carboxylic acids.

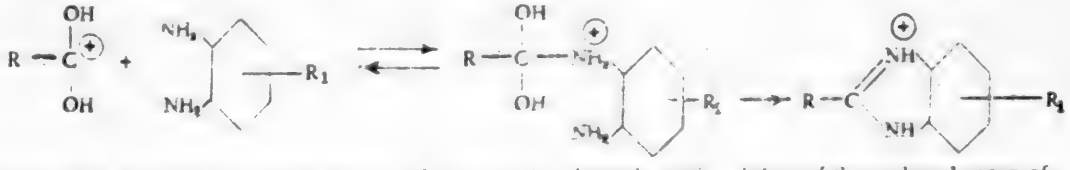
It seemed that the simplest method of preparing these compounds (II) would be polymeric condensation of 3,4-diaminobenzoic acid



(II)

Experiments carried out in this direction, however showed that 3,4-diaminobenzoic acid is not amenable to the same type of condensation.

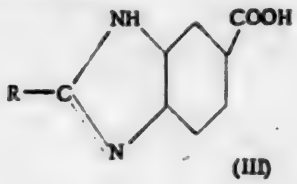
The cause of this inability becomes clear from the standpoint of the previously proposed [5] mechanism of condensation of carboxylic acid with an o-diamine in presence of mineral acid:



We see from this scheme that the success of this reaction depends on the ability of the carbonyl group of the carboxylic acid to polarize with formation of an electron deficiency at the carbon atom; this enables the o-diamine to combine at that carbon atom. It is natural that when the radical of the organic acid can compensate for this electron deficiency, the condensation in question proceeds with much greater difficulty. Even the benzene nucleus can exercise such an effect, so that benzoic acid only enters into this reaction in more drastic conditions than an aliphatic acid. In the case of p-aminobenzoic acid, however, conjugation enables the amino group to compensate for this electron deficiency to a considerably larger degree. Therefore, as we established, amino-

benzoic acid enters into condensation with o-phenylenediamine very sluggishly, forming the corresponding benzimidazole derivative in a yield of not more that 15% of the theoretical. In regard to the investigated 3,4-diaminobenzoic acid, the unfavorable effect on condensation of the amino group is even more marked than in the case of p-aminobenzoic acid.

Continuing our efforts to obtain the polybenzimidazole derivatives of interest to us, we resolved to weaken the harmful effect of the amino groups in 3,4-diaminobenzoic acid by acetylating them and converting the compound into derivatives of benzimidazole-5-carboxylic acid (III)



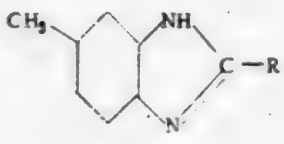
(III)

where: R = H, CH_3, C_6H_5.

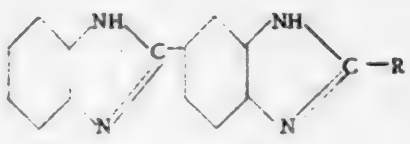
Subsequently, however, it was found much more convenient to prepare these compounds not from 3,4-diaminobenzoic acid but by oxidation of the more accessible derivatives of 5-methylbenzimidazole (IV), whose preparation has been described in a previous paper [6].

Our method of oxidation of the methyl groups of these compounds with chromic acid mixture gave close to the quantitative yield of products in all cases.

The theoretical considerations about the ability of acids (III) to condense with o-diamines were fully confirmed. In the very first experiments we obtained compounds with two benzimidazole groupings of the general formula (V)



(IV)

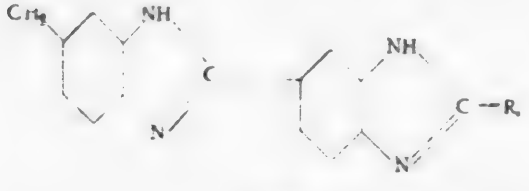


(V)

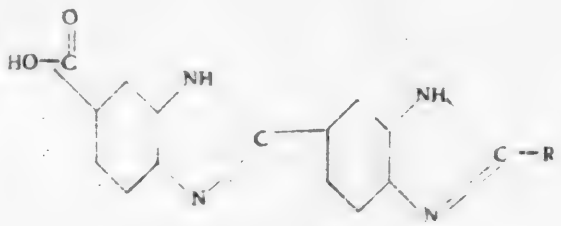
In this connection it is interesting to note that the behavior of benzimidazole carboxylic acids (III) in this reaction varies profoundly with the radical R. Thus, the most difficult of the investigated compounds to condense is the unsubstituted benzimidazole-5-carboxylic acid while the easiest to condense is 2-phenylbenzimidazole-5-carboxylic acid and the acid containing the CH_3 group occupies an intermediate position.

The structure of compounds of the type of (V) was confirmed by their synthesis from 2-diaminophenyl benzimidazole which was specially prepared, the latter was condensed with organic acids.

For the purpose of further lengthening of the chain, derivatives of benzimidazole-5-carboxylic acid were subjected to condensation with 3,4-toluylenediamine, and the resultant dibenzimidazole compounds, containing a methyl group (VI),



(VI)

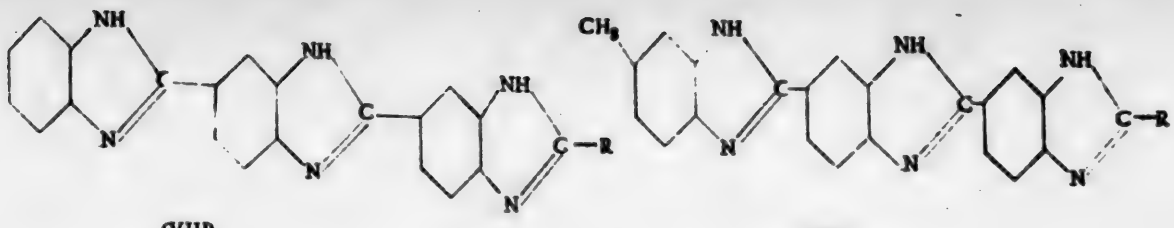


(VII)

were oxidized to the corresponding carboxylic acids (VII).

Their structure was confirmed by decarboxylation to the previously described compounds (V).

Condensation of these acids (VII) with o-phenylenediamine and 3,4-toluylenediamine gave compounds with three benzimidazole rings (VIII) and (IX): (See top of next page.)



(VIII) (IX)

In this case the character of the substituent R in the carboxylic acid (VII) naturally did not materially influence the course of the condensation. Due to the poor solubility of these compounds, the chain growth was stopped at this point.

Concerning the general properties of the prepared compounds, as was to be expected, the increasing size of the molecule and the transformation into more complex compounds was accompanied progressively by a fall in solubility and the compounds became more liable to form colloidal solutions; this was especially marked in the case of tribenzimidazole derivatives.

Spectral measurements showed for benzimidazoles an absorption maximum in the region of 2700-2800 A; for dibenzimidazoles one in the region of 3100-3200 A; and for tribenzimidazoles one in the region of 3400-3500 A. As we see the absorption maximum of these compounds gradually shifts toward the visible region. Visually, however, even tribenzimidazole derivatives are nearly colorless and only exhibit a faint yellow color with a weak intensity. Consequently, in this series we find confirmation of the known theory that imidazole derivatives are less highly colored than thiazoles.

EXPERIMENTAL

Benzimidazole-5-carboxylic Acid.

1.32 g 5-methylbenzimidazole is dissolved in 10 ml sulfuric acid (1:3); with heating to 100-103° and with stirring, dropwise addition is made of 2.4 g chromic acid in 10 ml sulfuric acid of the same concentration as before. 15 minutes after the completion of addition of the oxidizing agent, the reaction mass is cooled with ice water and the precipitated sulfate of benzimidazole-5-carboxylic acid is filtered off. The product is converted to the base by treatment with sodium acetate and is purified by crystallization from water to give 1-1.1 g acid with m.p. 300-325°.

2'-Benzimidazolyl-5'-benzimidazole.

1.62 g benzimidazole-5-carboxylic acid, 1.08 g o-phenylenediamine and 10 ml 20% hydrochloric acid are heated in a sealed tube at 180-200° for 4 hours. After cooling, the tube is opened and a considerable residual pressure is manifested (formation of carbon dioxide). The contents of the tube are neutralized with ammonia and the lilac-colored precipitate is filtered and washed with water. The precipitate is then purified in the form of the hydrochloride which is crystallized from concentrated hydrochloric acid. Yield 1.1-1.2 g colorless product with m.p. 362°. The base could not be obtained in the pure form because during crystallization it forms a gelatinous, unfilterable precipitate.

0.1255 and 0.1420 g substance: 0.2908 and 0.2835 g CO_2; 0.0447 and 0.0530 g H_2O; 0.1207 and 0.0964 g substance: 19.9 ml (19°, 755 mm) and 15.4 ml (19°, 757 mm) N_2; 0.1342 and 0.1308 g substance: 10 and 9.8 ml 0.086 N NaOH. Found %: C 54.53, 54.48; H 3.96, 4.17; N 18.3, 18.09; Cl 22.74, 22.87. $C_{14}H_{10}N_4 \cdot 2HCl$. Calculated %: C 54.72; H 3.91; N 18.24; Cl 23.12.

2-Methylbenzimidazole-5-carboxylic Acid.

Oxidation of 2,5-dimethylbenzimidazole to this carboxylic acid with chromic acid in sulfuric acid is carried out as in the previous case. The yield is 70-75% of the theoretical. The acid may be recrystallized from water for complete purification. M.p. 301-302°.

2-Methyl-5-(2'-benzimidazolyl)-benzimidazole.

1.70 g 2-methylbenzimidazole-5-carboxylic acid, 1.08 g o-phenylenediamine and 10 ml 20% hydrochloric acid are heated in a sealed tube for 40 minutes at 180-200°. The reaction mass is neutralized with ammonia, and the reaction product is filtered and crystallized from hydrochloric acid. Yield 2-2.5 g of dihydrochloride in the

form of colorless needles with m.p. 339-340°.

0.1368 and 0.1379 g substance: 0.2798 and 0.2823 g CO_2; 0.0578 and 0.0463 g H_2O. 0.1228 and 0.1311 g substance: 8.8 and 9.35 ml 0.086 N NaOH. Found %: C 55.77, 55.83; H 4.70, 3.91; Cl 21.88 and 21.76. $C_{15}H_{12}N_4 \cdot 2HCl$. Calculated %: C 56.07; H 4.36; Cl 22.20.

For the purpose of conversion to the base, the aqueous solution of the dihydrochloride is precipitated with ammonia and the precipitate crystallized from aqueous alcohol. M.p. 340°.

0.1013 and 0.1197 g substance. 0.2693 and 0.2970 g CO_2, 0.0455 and 0.0507 g H_2O. 0.0921 and 0.1174 g substance. 19.2 ml (19°, 742 mm) and 24.9 ml (18°, 748 mm) N_2. Found %: C 72.53, 72.15; H 5.02, 5.07; N 23.13, 21.11. $C_{15}H_{12}N_4$. Calculated %: C 72.56; H 4.84; N 22.58.

Addition of an ammoniacal solution of silver oxide to an alcoholic solution of the compound brings down a flocculent white precipitate of the silver salt of the compound, insoluble in water, alcohol and aqueous ammonia. After drying to constant weight, the silver content was determined by ignition:

1.0466 and 0.5068 g substance. 0.4916 and 0.2338 g Ag. Found %: Ag 46.97, 46.14. $C_{15}H_{10}N_4Ag_2$. Calculated %: Ag 46.72.

The lemon-yellow picrate is precipitated by running together an alcoholic solution of the compound with an alcoholic solution of picric acid. It melts sharply at 282-282.5°. The product contains two molecules of picric acid per molecule of compound:

0.0822 and 0.0857 g substance: 14.5 ml (19°, 735 mm) and 15.2 ml (20°, 753 mm) N_2. Found%: N 19.54, 19.65. $C_{15}H_{12}N_4 \cdot 2C_6H_3N_3O_7$. Calculated %: N 19.83.

2,5'-Dimethyl-5-(2'-benzimidazolyl)-benzimidazole

1.22 g 3,4-toluylenediamine, 1.76 g 2-methylbenzimidazole-5-carboxylic acid and 10 ml 20% hydrochloric acid are heated in a sealed tube for 4 hours at 180-200°. The product is isolated as in the preceding preparation and is purified in the form of the base by crystallization from 50% alcohol. The melting point is high and indefinite.

0.0966 and 0.1620 g substance: 0.2606 and 0.4368 g CO_2, 0.0492 and 0.0824 g H_2O. 0.1036 and 0.1111 g substance: 9.9 ml (18°, 749 mm) and 20.4 ml (19°, 751 mm) N_2. Found %: C 73.60, 73.54; H 5.70, 5.74; N 21.60, 20.85. $C_{16}H_{14}N_4$. Calculated %: C 73.28; H 5.34; N 21.37.

The base is converted to the hydrochloride by crystallization from 20-25% hydrochloric acid. The colorless, fine crystals of the salt melt at above 300°.

0.1795 and 0.1773 g substance: 12.4 and 11.95 ml 0.086 N NaOH. Found %. Cl 21.11, 20.6. $C_{16}H_{14}N_4 \cdot 2HCl$. Calculated %. Cl 21.19.

The bright-yellow picrate comes down immediately on running together alcoholic solutions of the substance and picric acid. M.p. (sharp) 274°.

2-Methyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole

Oxidation of 2,5'-dimethylbenzimidazolyl-benzimidazole to the carboxylic acid is performed with chromic acid in the same condition as in preceding preparations. The sulfate of the reaction product is dissolved in aqueous ammonia and treated with hydrochloric acid to bring down the hydrochloride and the latter is crystallized from 10-15% hydrochloric acid. The colorless hydrochloride melts at about 350°.

0.1489 and 0.1259 g substance: 0.2847 and 0.2304 g CO_2, 0.0555 and 0.0441 g H_2O. 0.1732 and 0.1648 g substance: 22.9 ml (19°, 757 mm) and 22.2 ml (20°, 760 mm) N_2. 0.1170 and 0.1693 g substance: 7.1 and 10.4 ml 0.086 N NaOH. Found %: C 52.18, 52.06; H 4.07, 4.08, N 15.25, 15.23, Cl 19.38, 18.76. $C_{16}H_{12}N_4O_2 \cdot 2HCl$. Calculated %: C 52.60; H 3.83, N 15.35, Cl 19.45.

For the purpose of confirming its structure, the acid was decarboxylated. A well-triturated mixture of 0.5 g substance and 3 g soda lime was heated for 10 hours at 280-300°. After solution in water and acidification, the isolated product of reaction was purified by crystallization from aqueous alcohol. The picrate has m.p. 274° and does not give a depression with the picrate of the above-described 2-methyl-benzimidazolyl-benzimidazole.

2-Methyl-5-[2'-benzimidazolyl-5'-(2''-benzimidazolyl)]-benzimidazole

Preparation is performed by condensing 3.7 g of the hydrochloride of the above-described acid with 1 g

o-phenylenediamine in 10 ml 15% hydrochloric acid by heating in a sealed tube for 4 hours at 180-200°. The product brought down by treatment of the reaction mass with ammonia is purified by crystallization from dilute hydrochloric acid. Yield about 3.5 g faint yellow hydrochloride. M.p. above 360°.

0.1486 g and 0.1767 g substance: 0.3002 and 0.3573 g CO_2; 0.0802 and 0.0685 g H_2O. 0.1496 and 0.1582 g substance: 23.6 ml (22°, 765 mm) and 24.8 ml (22°, 764 mm) N_2. 0.1417 and 0.1516 g substance: 10.25 and 11.1 ml 0.086 N NaOH. Found %: C 55.17, 55.10; H 4.53, 4.33; N 18.17, 18.02; Cl 22.01, 22.35. $C_{28}H_{18}N_6 \cdot 3HCl$. Calculated %: C 55.75; H 3.01; N 17.74; Cl 22.49.

2,5'-Dimethyl-5-[2'-benzimidazolyl-5'-(2"-benzimidazolyl)]benzimidazole

The product was prepared similarly to the preceding preparation by condensation of the acid with 3,4-tolylenediamine and was purified by crystallization from dilute hydrochloric acid. Yield 85-90% of the theoretical. M.p. about 400°.

0.1168 and 0.1332 g substance: 0.2416 and 0.2741 g CO_2; 0.0480 and 0.0544 g H_2O. 0.1414 and 0.1511 g substance: 21.2 ml (21°, 766 mm) and 22.5 ml (22°, 768 mm) N_2. 0.1060 and 0.1431 g substance: 7.5 and 10.1 ml 0.086 N NaOH. Found %: C 56.44, 56.15; H 4.59, 4.57; N 17.34, 17.14; Cl 21.60, 21.54. $C_{28}H_{20}N_6 \cdot 2HCl$. Calculated %: C 56.59; H 4.31; N 17.23; Cl 21.84.

2-Phenylbenzimidazole-5-carboxylic Acid

15 g 2-phenyl 5-methylbenzimidazole is dissolved in 300 ml concentrated sulfuric acid and the solution gradually diluted with 600 ml water. Into the boiling solution is gradually run a solution of 18 g chromic acid in 30 ml water. A violent reaction takes place, at the conclusion of which the sulfate of the carboxylic acid crystallizes out from the still boiling solution. The reaction mass is cooled and diluted with 600 ml water, the product is filtered and washed with water. It is purified by reprecipitation with hydrochloric acid from the ammoniacal solution and by crystallization from dilute hydrochloric acid. Yield 16 g hydrochloride of the carboxylic acid. Long, colorless needles (from dilute hydrochloric acid) m.p. 304-305°. The acid is readily soluble in dilute ammonia and in sodium carbonate solution; it is precipitated from solution by hydrochloric and sulfuric acids, and less readily by acetic acid, in the form of the respective salts.

The hydrochloride of this compound was subjected to potentiometric titration with the glass electrode; for this purpose 0.1500 g was dissolved in 12 ml 0.1 N caustic alkali and titrated with 0.1 N hydrochloric acid. Two potential jumps were obtained, the first corresponding to the instant of absence of free alkali from the solution after addition of 0.75 ml 0.1 N hydrochloric acid (pH 8.4) and the second (weaker) corresponding to the appearance in the solution of free hydrochloric acid after addition of 6.4 ml 0.1 N hydrochloric acid.

Found: according to the first point (12 ml − 0.75 ml = 11.25 ml); equivalent weight = 133.3; according to the first and second points (6.4 ml − 0.75 ml = 5.65 ml), mol. wt. 267. $C_{14}H_{10}O_2N_2 \cdot HCl$. Calculated: mol. wt. 274.5, equiv. wt. 137.25.

0.1084 g substance: 9.4 ml N_2 (15°, 760 mm). 0.1495 g substance: 5.5 ml 0.1 N solution $AgNO_3$. Found %: N 10.34, Cl 13.00. $C_{14}H_{10}O_2N_2 \cdot HCl$. Calculated %: N 10.20; Cl 12.95.

2-Phenyl-5-[2'-benzimidazolyl]-benzimidazole

2.75 g 2-phenylbenzimidazole-5-carboxylic acid hydrochloride and 1.5 g o-phenylenediamine are heated in a sealed tube with 10 ml 15% hydrochloric acid for 6 hours at 180-200°. The precipitate is filtered and twice treated with ammonia solution while hot to remove traces of carboxylic acid. The product is purified by several crystallizations from dilute hydrochloric acid, during this operation addition is made to the first hot crystallization solution of a very small amount of chromic acid solution to decompose the blue dye formed by a secondary reaction. Yield 3 g. Fine colorless needles (from dilute hydrochloric acid, with [illegible]). The product is soluble on heating in dilute hydrochloric acid and is salted out by an excess of it.

The free base is obtained by treating the hydrochloride with ammonia; it crystallizes from aqueous alcohol in fine, white needles. M.p. 308-310°. The base is insoluble in dilute acetic acid.

Analysis of the base:

0.1024 g substance: 0.2910 g CO_2; 0.0425 g H_2O. 0.0655 g substance: 10 ml N_2 (12°, 762 mm). Found %: C 77.37; H 4.62; N 18.[illegible]. $C_{20}H_{14}N_4$. Calculated %: C 77.42; H 4.52; N 18.05.

Analysis of the hydrochloride:

0.0752 g substance: 10.5 ml N_2 (18°, 760 mm). 0.1003 g substance: 2.85 ml 0.1 N solution $AgNO_3$. Found %: N 16.33; Cl 10.10. $C_{20}H_{13}N_4Cl$. Calculated %: N 16.15; Cl 10.25.

2-Phenyl-5-(5'-methyl-2'-benzimidazolyl)-benzimidazole

5 g 2-phenylbenzimidazole-5-carboxylic acid hydrochloride and 3.7 g 3,4-toluylenediamine are heated in a sealed tube with 20 ml 15% hydrochloric acid for 6 hours at 180-200°. The product is worked up and purified in the same way as the preceding preparation. Yield 4.7 g. Fine, colorless needles (from dilute hydrochloric acid), m.p. 311-315°.

The free base crystallizes from aqueous alcohol in fine needles with m.p. 329-331°. The base is insoluble in dilute acetic acid.

Analysis of the base:

0.1051 g substance: 0.2971 g CO_2 and 0.0473 g H_2O. 0.0832 g substance: 12.1 ml N_2 (14°, 764 mm). Found %: C 77.80; H 5.04; N 17.48. $C_{21}H_{16}N_4$. Calculated %: C 77.78; H 4.93; N 17.27.

Analysis of the hydrochloride:

0.1505 g substance: 4.2 ml 0.1 N solution $AgNO_3$. Found %: Cl 9.68. $C_{21}H_{17}N_4Cl$. Calculated %: Cl 9.83.

2-Phenyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole

4 g 2-phenyl-5-(5'-methyl-2'-benzimidazolyl)-benzimidazole is dissolved in 160 ml concentrated sulfuric acid and the solution is gradually diluted with 240 ml water. Into the boiling solution is gradually run a solution of 2.8 g chromic acid in 10 ml water. At the conclusion of the reaction, the sulfate of the carboxylic acid crystallizes from the still-boiling solution. The reaction mass is cooled and diluted with 500 ml water, the product is filtered off and well washed with water.

The product is purified by three reprecipitations with hydrochloric acid from hot ammoniacal or sodium carbonate solution and thoroughly washed with water. Yield 3.5-4 g of the hydrochloride of the carboxylic acid.

Fine, barely yellow needles with m.p. 314-319°. The acid dissolves with heating in dilute ammonia and sodium carbonate solution and is brought down by hydrochloric, sulfuric and acetic acids. The salt of the acid is readily isolated from solution by adding sodium chloride solution. Soluble in alcohol.

0.1500 g acid was dissolved in 12 ml 0.1 N caustic alkali and subjected to potentiometric titration with 0.1 N hydrochloric acid using a glass electrode. Two potential jumps were obtained, the first corresponding to the instant of titration of the excess alkali after addition of 4.2 ml hydrochloric acid (pH 8.8) and the second corresponding to the appearance of free hydrochloric acid after addition of 8 ml 0.1 N hydrochloric acid.

Found according to the first point: (12 ml − 4.2 ml = 7.8 ml), equiv. wt. 192.3; according to the first and second points: (8 ml − 4.2 ml = 3.8 ml), mol. wt. 395. $C_{21}H_{14}O_2N_4 \cdot HCl$. Calculated: mol. wt. 390.5; equiv. wt. 185.25.

0.0985 g substance: 12 ml N_2 (18°, 744 mm). Found %: N 14.36. $C_{21}H_{15}O_2N_4Cl$. Calculated %: N 14.34.

2-Phenyl-5-[2'-benzimidazolyl-5'-(2''-benzimidazolyl)]-benzimidazole

1.5 g 2-phenyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole and 0.75 g o-phenylenediamine are heated with 15 ml 10% hydrochloric acid in a sealed tube at 200-220° for 10 hours. The precipitate is filtered, washed with water, and twice treated with sodium carbonate solution with heating for removal of residues of carboxylic acid. The product is purified by dissolving in dilute acetic acid and precipitating as the dihydrochloride by addition to the hot solution of concentrated hydrochloric acid. The purification is repeated several times. The first time a few drops of chromic acid solution are added with the hydrochloric acid to decompose the dye. Yield 1.2 g. Barely yellowish slender long needles of hydrochloride, darkening slightly but not melting even at 360°. Almost insoluble in water and organic solvents.

0.2021 g substance: 31.4 ml N_2 (18°, 742 mm); 0.1500 g substance: 6.0 ml 0.1 N solution $AgNO_3$. Found %: N 16.88; Cl 14.15. $C_{27}H_{18}N_6 \cdot 2HCl$. Calculated %: N 16.80; Cl 14.20.

2-Phenyl-5-[2'-benzimidazolyl-5'-(5''-methyl-2''-benzimidazolyl)]-benzimidazole

3 g 2-phenyl-5-(5'-carboxy-2'-benzimidazolyl)-benzimidazole and 1.5 g 3,4-toluylenediamine are heated with 20 ml 10% hydrochloric acid in a sealed tube at 200-220° for 16-20 hours. The product is separated and purified as

above. Yield 1.8 g. The barely yellow, slender, long needles of the dihydrochloride darken, but do not melt even at 360°. Almost insoluble in water and organic solvents.

The base is obtained by treatment of the salt with ammonia. It is likewise nearly insoluble in organic solvents but dissolves readily in aqueous acetic acid to form a salt, and it may be isolated from solution by adding hydrochloric acid or even sodium chloride solution.

0.0610 g substance: 8.2 ml N_2 (16°, 770 mm). 0.1002 g substance: 0.0557 g AgCl. 0.1500 g substance: 5.6 ml 0.1 N $AgNO_3$. Found %: N 16.1; Cl 13.6, 13.7. $C_{28}H_{28}N_6 \cdot 2HCl$. Calculated %: N 16.4; Cl 13.8.

Experiments on Condensation of 3,4-Diaminobenzoic Acid

2.25 g 3,4-diaminobenzoic acid hydrochloride is heated with 10 ml 20% hydrochloric acid in a sealed tube at 180-200° for 40 minutes. A fairly high pressure was always present in the tubes after completion of the reaction. The contents of the tubes are filtered and the solid crystallized several times from 10% hydrochloric acid. Yield 0.1 g, m.p. 325-330°. The yield increases slightly if 1 g o-phenylenediamine is added to the tube before the reaction.

The resultant 3,4-diaminophenylbenzimidazole absorbs nitrous acid without forming a diazo compound. In acetic acid solution it gives with phenanthrenequinone a copious green precipitate with the characteristic reactions for phenanthrazines.

For confirmation of its structure, the product was condensed with formic acid and with acetic acid. 1 g product and 0.5 ml acid were heated in 5 ml 20% hydrochloric acid at 180-200° for 40 minutes. The resultant compound, containing two benzimidazole groupings, were purified in the form of the hydrochlorides and found to be identical with these previously described derivatives in respect to melting points and the melting points of their picrates (no depression in mixed melting tests).

SUMMARY

1. Products of a new and previously undescribed type—linearly arranged polybenzimidazole derivatives—may be prepared by various routes of which the best is condensation of a carboxylic acid with o-toluylenediamine followed by oxidation of the methyl group of the formed imidazole derivative to carboxyl and further condensation with an aromatic o-diamine. By this method substances are obtained containing two and three benzimidazole groupings in a line.

2. The prepared compounds compared with the known primuline dyes containing similarly arranged benzothiazole rings have not so deep a color.

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* See Consultants Bureau English translation page 725 ff.
** See Consultants Bureau English translation page 1555.

IMIDAZOLE DERIVATIVES

VII. PREPARATION OF BENZIMIDAZOLE SULFONIC ACIDS BY THE SINTERING METHOD [1]

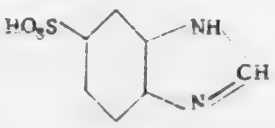
L. S. Efros

Treatment of benzimidazole derivatives with concentrated sulfuric acids gives the corresponding sulfonic acids which, according to the literature [2], may be used as emulsifying agents.

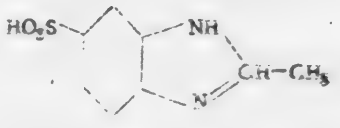
We have succeeded in also preparing the sulfonic acids of these compounds by another method, which consists in the sintering of their acid sulfates. Hitherto, this method was known only for the preparation of sulfonic acids of mainly aromatic amines and has never been applied for the introduction of the sulfo group into heterocyclic systems.

In the present case, as well as generally in processes of sintering, during heating of the sulfates of benzimidazol derivatives at above the melting point, water is first evolved and sulfamic acids are apparently formed which are easily hydrolyzed by water. Consequently, if the melt is poured into water after completion of this stage of the reaction, the original benzimidazole can be very easily isolated by neutralization. On further heating of the melt, however, these intermediate products are smoothly transformed into the usual sulfonic acids.

By this method we obtained good yields of the sulfonic acids of benzimidazole(I) and 2-methylbenzimidazole (II).



(I)



(II)

(III)

The position of the sulfo group in them was confirmed by their synthesis by the condensation of 1,2-phenylenediamine-4-sulfonic acid (III) with formic and acetic acids by the previously described method [3].

In passing from the above benzimidazole derivatives to compounds with more complex substituents in the 2 position the sintering reaction is very seriously hindered, the yields fall, and the preparation of sulfonic acids from them by the sinter method no longer presents practical value.

As was shown earlier [4] there are specific features about the chemical behavior of benzimidazole and its derivatives which can only be explained on the basis of the structure of the molecule of these compounds as a whole. Moreover, the reaction under consideration reveals the close relation between these compounds and aromatic amines of the benzene series.

EXPERIMENTAL

Benzimidazole-5-sulfonic Acid

Preparation by the method of sintering of benzimidazole sulfate. The sulfate is prepared from 11.8 g base with m.p. 170° (0.1 mole) which is thoroughly triturated in a mortar with 6 ml concentrated sulfuric acid (s.g. 1.84) (0.12 mole). The initially hot liquid mass rapidly solidifies. It is transferred to a porcelain funnel and well washed with ether at the pump. After drying, about 19 g crystalline benzimidazole sulfate is obtained.

0.1081 and 0.1075 g substance: 0.1173 and 0.1170 g $BaSO_4$. Found %: H_2SO_4 45.6, 45.8.
$C_7H_6N_2 \cdot H_2SO_4$. Calculated %: H_2SO_4 45.3.

5 g of the so prepared benzimidazole sulfate is placed in a short test tube of maximum width and heated on an oil bath at 220-240° until water vapor ceases to come off. The bath temperature is then raised to 260-280° and heating continued until a specimen of the melt when dissolved in water no longer deposits benzimidazole when ammonia is added. The melt is crystallized from a very small amount of water to give 4-4.5 g

benzimidazole-5-sulfonic acid in the form of colorless needles with m.p. 365-367° (after 3-4 crystallizations). The product is readily soluble in aqueous ammonia and soda, less soluble in water, and poorly soluble in alcohol.

0.0988 and 0.1005 g substance: 12.0 and 12.3 ml N_2 (18°, 758 mm). 0.1220 g substance: 0.1467 g $BaSO_4$. Found %: N 14.20, 14.32; S 16.50. $C_7H_6O_3N_2S$. Calculated %: N 14.13, S 16.15.

Preparation by condensation of 1,2-phenylenediamine-4-sulfonic acid with formic acid. 1.12 g phenylenediamine-sulfonic acid (0.005 mole), 1 ml formic acid and 5 ml water are heated in a sealed tube at 180-190° for 40 minutes. After cooling, the tube is opened and the crystals are filtered. Yield 0.95 g. After several crystallizations from a small amount of water, the product is obtained as needles with m.p. 365-367°. A mixed sample with the sulfonic acid prepared as above melts at the same temperature.

2-Methylbenzimidazole-5-Sulfonic Acid

Preparation by sintering of 2-methylbenzimidazole sulfate. The sulfate was prepared in the same way as benzimidazole sulfate.

0.1173 and 0.1157 g substance: 10.1 and 9.9 ml 0.1 N NaOH. Found %: H_2SO_4 42.2, 42.7. $C_8H_8N_2 \cdot H_2SO_4$. Calculated %: H_2SO_4 42.6.

Sintering of this sulfate is effected as in the preceding case, except that a longer period is required and the temperature has to be raised to 280-290°. The yield of 2-methylbenzimidazole-5-sulfonic acid is 2-2.5 g from 5 g salt (about 50% of the theoretical). The substance forms colorless needles, very soluble in hot water, less soluble in cold water and insoluble in alcohol. The m.p. is very high and indefinite.

0.1012 and 0.1025 g substance: 11.5 and 11.7 ml N_2 (18°, 758 mm). 0.1597 g substance: 0.1712 g $BaSO_4$. Found %: N 13.3, 13.35; S 14.70. $C_8H_8O_3N_2S$. Calculated %: N 13.26; S 15.08.

Preparation by condensation of 1,2-phenylenediamine-4-sulfonic acid with acetic acid. 1.12 g phenylenediamine-sulfonic acid (0.005 mole), 1 ml acetic acid and 5 ml water are heated in a sealed tube at 180-190° for 40 minutes. This reaction gave 1 g of a product whose outward appearance, solubility in water and alcohol and behavior on heating in a capillary were entirely reminiscent of the properties of the product obtained by the sinter method.

0.1461 g substance: 0.1597 g $BaSO_4$. Found %: S 14.98. $C_8H_8O_3N_2S$. Calculated %: S 15.08.

SUMMARY

The method of sintering of sulfates of benzimidazole and 2-methylbenzimidazole was applied to the preparation of the sulfonic acids of these compounds, thus demonstrating the possibility of application of this method also to the synthesis of sulfonic acids of certain heterocyclic compounds.

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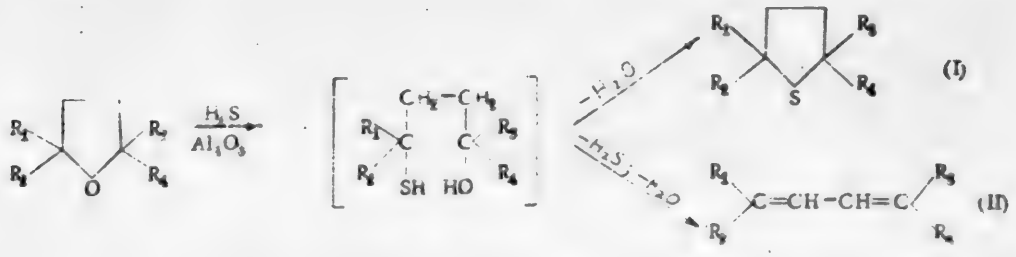
TRANSFORMATION OF 3,3-DIMETHYLTETRAHYDROFURAN INTO 3,3-DIMETHYLTETRAHYDROTHIOPHENE AND 3,3-DIMETHYLPYRROLIDINE. XI.

Yu. K. Yuryev, G. Ya. Kondratyeva and N. K. Sadovaya

In a previous investigation it was shown that homologs of tetrahydrofuran, in the conditions of catalytic transformation of oxygenated heterocycles into rings with other heteroatoms, are transformed —depending on the number, magnitude and position of the methyl groups in the ring—either into the corresponding homologs of tetrahydrothiophene or into diene hydrocarbons or into a mixture of both compounds.

2,2,5,5-Tetraalkyltetrahydrofurans only gave a mixture of diene hydrocarbons with various positions of the double bonds in presence of alumina in a hydrogen sulfide atmosphere [1]. When 2,2-dimethyltetrahydrofuran was led over the catalyst in the same conditions, two competing reactions took place simultaneously: dehydration of the oxygen-containing heterocycle with formation of unsaturated hydrocarbons and transformation into 2,2-dimethyltetrahydrothiophene.

It is clear that the usual reaction of replacement of the bridge oxygen by another heteroatom is suppressed in the case of 2,2-disubstituted tetrahydrofurans. Dialkyltetrahydrofurans with another structure, namely 2,5-dimethyltetrahydrfuran [2] and 2,4-dimethyltetrahydrofuran [3], react normally and are transformed in good yield into 2,5- and 2,4-dimethyltetrahydrothiophene, respectively. The first stage in the transformation of oxygen-containing heterocycles into sulfur-containing ones (rupture of the ring at the carbon-oxygen linkage) with addition of the elements of hydrogen sulfide undoubtedly proceeds identically in all compounds of the tetrahydrofuran series, but the direction of the subsequent dehydration of the intermediately formed 1,4-mercaptooxy compound is determined by the peculiarities of its structure.



In the case of formation of diterriary 1,4-mercaptooxy compounds from 2,2,5,5-tetraalkyltetrahydrofurans, the process takes place exclusively according to scheme (II) i.e., with simultaneous cleavage of water and hydrogen sulfide, and leads to diene hydrocarbons. In the case of primary-tertiary 1,4-mercaptoalcohols ($R_1=R_2=H$), the reaction proceeds simultaneously in the two possible directions (I) and (II), and gives a mixture of dienes (products of dehydration and hydrogen sulfide cleavage) and the corresponding tetrahydrothiophene homolog. Finally, disecondary ($R_2=R_4=H$) and primary-secondary ($R_1=R_2=R_4=H$) 1,4-mercaptooxy compounds —like diprimary ones (formed from tetrahydrofuran in which $R_1=R_2=R_3=R_4=H$) —normally undergo dehydration to tetrahydrothiophene homologs.

Alkyl radicals located at the β-carbon atom of tetrahydrofuran excercise the least influence on the yield of the corresponding tetrahydrothiophene homolog, and 3-alkyltetrahydrofurans are transformed into 3-alkyltetrahydrothiophenes only with slightly lower yields than tetrahydrofuran itself. 3-methyltetrahydrofuran gives 3-methyltetrahydrothiophene in a yield of 80% [4], while tetrahydrothiophene is obtained from tetrahydrofuran in a yield of 90% [5]. Attention is also drawn to the fact that 3-alkyltetrahydrothiophenes are formed from 3-alkyltetrahydrofurans in better yields than are the corresponding α-alkyltetrahydrothiophenes from α-alkyltetrahydrofurans[6].

The transformation of tetrahydrofuran homologs into pyrrolidine homologs is marked by the same regularities, but the yield of pyrrolidine homologs is lower than the yield of their sulfur-containing analogs.

In this investigation we examined the transformation of 3,3-dimethyltetrahydrofuran into the corresponding nitrogen- and sulfur-containing heterocyclic compounds. It was established that the presence of two methyl radicals

at one and the same carbon atom of the ring did not hinder the transformation of 3,3-dimethyltetrahydrofuran into 3,3-dimethyltetrahydrothiophene (yield 73%) and into 3,3-dimethylpyrrolidine (yield 41%).

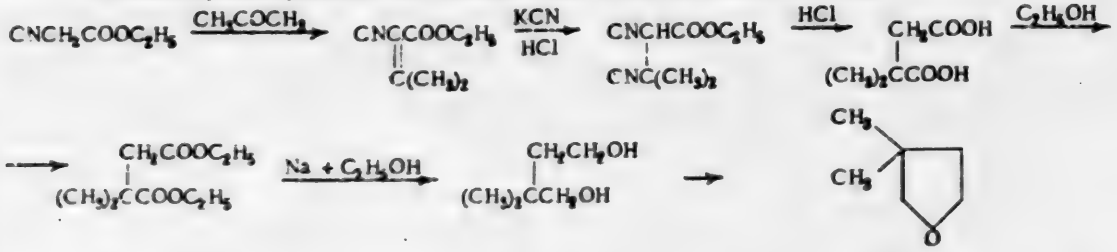
Regarding 3,3-dimethyltetrahydrofuran itself, we must note that the literature contains erroneous statements. In describing the reduction of the diethyl ester of α,α-dimethylsuccinic acid with sodium in ethyl alcohol, Blanc [6] reported that he isolated from the reaction mixture a few milliliters of a substance with b.p. 85° which did not mix with water and possessed an acetone-like odor. Blanc suggested that this substance was 3,3-dimethyltetrahydrofuran, although the data of the elementary analysis deviated considerably from those calculated for 3,3-dimethyltetrahydrofuran.

After preparing 3,3-dimethyltetrahydrofuran in the pure state, we were convinced that Blanc's suggestion was erroneous, the constants and properties of 3,3-dimethyltetrahydrofuran are entirely different from those of the substance isolated by Blanc.

EXPERIMENTAL

1 Preparation of 3,3-Dimethyltetrahydrofuran

3,3-Dimethyltetrahydrofuran was prepared by the following series of reactions:



a) Ethyl ester of α,β-dicyano β-methylbutyric acid [7]: b.p. 152-156° (22 mm); n_D^{20} 1.4382; d_4^{20} 1.0486; MR_D 45.13 $C_9H_{12}O_2N_2$ Calculated MR_D 45.05.

Literature data: b.p. 136-141° (9 mm) [7].

b) α,α-Dimethylsuccinic acid was prepared by hydrolysis of the ethyl ester of α,β-dicyano-β-methylbutyric acid [7]: b.p. 139-140°. Yield 75% of the theoretical.

Literature data: b.p. 138-139° [7]; b.p. 141-142° [8]; b.p. 139-140° [9].

c) Diethyl ester of α,α-dimethylsuccinic acid was prepared from α,α-dimethylsuccinic acid and absolute alcohol by saturation with hydrogen chloride [10]; b.p. 101° (15 mm), n_D^{20} 1.4233, d_4^{20} 0.9936; MR_D 51.84 $C_{10}H_{18}O_4$ Calculated MR_D 51.69 Yield 62% of the theoretical.

Literature data: b.p. 101° (15 mm) [8]; b.p. 215°, n_D^{20} 1.421; d_4^{20} 0.994 [11].

d) 2,2-Dimethylbutanediol-1,4 was prepared by reduction of the diethyl ester of α,α-dimethylsuccinic acid with sodium in absolute alcohol [12]: b.p. 117° (8 mm), n_D^{20} 1.4513, d_4^{20} 0.9739; MR_D 32.63. $C_6H_{14}O_2$ Calculated MR_D 32.96 Yield 69% of the theoretical.

Literature data: b.p. 123° (9 mm), d_0^4 0.996 [12].

e) 3,3-Dimethyltetrahydrofuran A mixture of 9.2 g 2,2-dimethylbutanediol-1,4 and 0.9 g finely triturated aluminosilicate catalyst was heated in a distillation flask at 180-190°. The distillate was saturated with potassium carbonate and the 3,3-dimethyltetrahydrofuran (which floated to the surface) was dried with calcium chloride and distilled through a column. Two distillations over sodium gave pure 3,3-dimethyltetrahydrofuran with b.p. 98.99 (750 mm), n_D^{20} 1.4121, d_4^{20} 0.8455, MR_D 29.44. $C_6H_{12}O$. Calculated MR_D 29.35.

Found %: C 71.28, 71.46; H 12.15, 12.12. $C_6H_{12}O$. Calculated %: C 71.99; H 12.09. Yield 95% of the theoretical. 3,3-Dimethyltetrahydrofuran has not been described in the literature.

2 Transformation of 3,3-Dimethyltetrahydrofuran into 3,3-Dimethyltetrahydrothiophene

16.6 g 3,3-dimethyltetrahydrofuran was passed over alumina in a stream of hydrogen sulfide at 350° with a velocity of 10 drops/min. The catalyzate was collected in a well-cooled receiver and was saturated with solid KOH and extracted with ether. After driving off the ether, the reaction product was distilled through a column to give a

fraction with b.p. 143-146° (755 mm). After a second distillation over sodium, the 3,3-dimethyltetrahydrothiophene possessed the following constants: b.p. 144-145° (755 mm); n_D^{18} 1.4861; d_4^{18} 0.9374; MR_D 35.55. $C_6H_{12}S$. Calculated MR_D 35.40. The melting point of the $HgCl_2$ compound is 148°.

Found %: C 61.98, 62.01; H 10.30, 10.21; S 27.60, 27.59. $C_6H_{12}S$. Calculated %: C 62.05; H 10.35; S 27.59.

Yield 8.9 g (73% of the theoretical). 3,3-Dimethylthiophane has not been described in the literature.

3. Transformation of 3,3-Dimethyltetrahydrofuran into 3,3-Dimethylpyrrolidine

10.2 g 3,3-dimethyltetrahydrofuran was passed over activated Al_2O_3 in a stream of ammonia at 325° with a velocity of 6 drops/min. The catalyzate was saturated with solid NaOH and extracted with ether. The ether extract was dried with KOH, the ether was driven off and the residue distilled through a column. The first distillation gave a fraction with b.p. 100-110°. After a second distillation the 3,3-dimethylpyrrolidine had the constants: b.p. 110-111° (760 mm); n_D^{18} 1.4386; d_4^{18} 0.8422; MR_D 30.95. $C_6H_{13}N$. Calculated MR_D 31.31. Yield 4.2 g (41% of the theoretical).

The picrate (recrystallized from alcohol) had m.p. 158°.

Found %: N 17.51. $C_{12}H_{16}O_7N_4$. Calculated %: N 17.57.

3,3-Dimethylpyrrolidine has not been described in the literature.

SUMMARY

1. The 3,3-dimethyltetrahydrofuran described in this paper differs considerably from the substance erroneously assumed by Blanc to be 3,3-dimethyltetrahydrofuran.

2. It was established that 3,3-dimethyltetrahydrofuran is smoothly transformed into 3,3-dimethyltetrahydrothiophene in the conditions of catalytic transformation of oxygen-containing heterocycles into rings containing other heteroatoms.

3. By means of the indicated reaction 3,3-dimethyltetrahydrofuran is also transformed into 3,3-dimethylpyrrolidine.

4. It was established that when two methyl groups are present at one and the same carbon atom in the β-position of the tetrahydrofuran ring the catalytic transformation of the oxygen-containing heterocycle only proceeds in the direction of formation of cyclic systems with other heteroatoms.

5. The introduction of a second methyl group in the β position of the tetrahydrofuran ring has considerably less influence on the yield of nitrogen- and sulfur-containing products of catalytic transformation of heterocycles than the introduction of the first methyl group.

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THE ACTION OF AROMATIC DIAZO COMPOUNDS ON COMPOUNDS OF THE TYPE OF ALKYLACETOACETIC ESTERS AS A METHOD OF PREPARATION OF ARYLHYDRAZINES OF KETO ACIDS, α-AMINO ACIDS AND NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS

XV. SYNTHESIS OF D L-GLUTAMIC ACID

V. V. Feofilaktov and N. K. Semenova

Glutamic acid was first isolated from the hydrolyzate of vegetable protein by Ritthausen [1], who also proposed for it the structural formula which was later confirmed by Dittmar [2], Markovnikov [3] and Wolff. The latter effected its synthesis [4]. A series of synthetic methods for its preparation are known and may be divided broadly into four groups: those based on reduction of α-nitrosoglutaric acid or its esters, prepared by various routes; synthesis using α-ketoglutaric acid; syntheses by the Strecker-Zelinsky method; and syntheses on the basis of amino-malonic ester.

Wolff [4] was the first to prepare glutamic acid from the nitrosoglutaric acid derived from levulinic acid. This synthesis is only of historical interest. McIlwain and Richardson [5] obtained nitrosoglutaric acid from α-acetoglutaric ester, which, in turn, was prepared from α-chloropropionic and acetoacetic esters by a slight modification of the method of Clemo and Welch [6]; they prepared glutamic acid from nitrosoglutaric acid in a yield of 39% reckoned on the original chloropropionic ester. Hamlin and Hartung [7] raised the yield by the same method to 74% by conducting the reduction in presence of platinum oxide at a hydrogen pressure of 10 atmospheres, and thereby rendered this method suitable for preparative purposes.

The difficultly accessible α-ketoglutaric acid is the starting material in several methods [8, 9] which are devoid of preparative value. In the same class are also the syntheses of Keimatsu and Sugasawa [10, 11] by the Strecker-Zelinsky method from β-formylpropionic acid and its esters which are derived from acrolein.

Alkylation of aminomalonic ester with β-chloropropionic ester did not give a high yield of glutamic acid; the yields could be considerably improved, however, by alkylating benzaminomalonic ester with β-bromopropionic ester, and this method is suitable for preparative purposes [13].

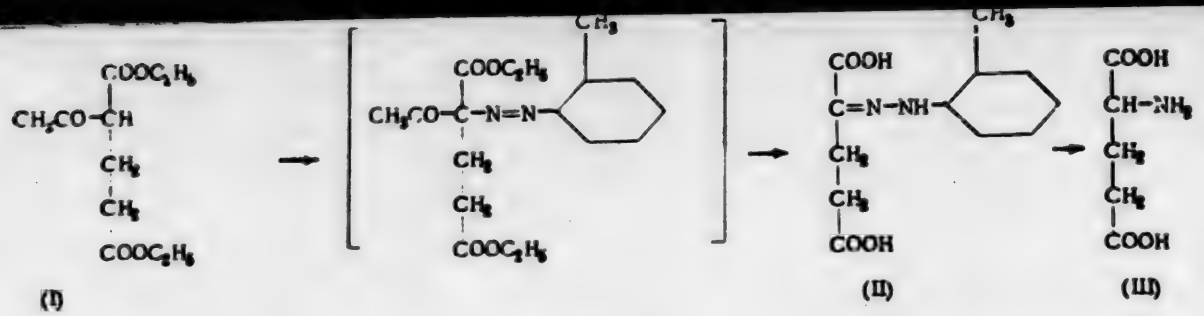
Acetaminomalonic ester was alkylated with acrylonitrile [14] or with methacrylonitrile [15]; subsequent hydrolysis and decarboxylation gave glutamic acid in good yields. Phthaliminomalonic ester was alkylated [16] with β-chloropropionic ester or with methyl acrylate, hydrolysis (requiring drastic conditions) and decarboxylation of the intermediate products gave glutamic acid in good yields.

Of the syntheses described the simplest is the one utilizing the relatively accessible α-acetoglutaric ester. There are difficulties, however, in connection with its nitrosation with alkyl nitrite or nitrosylsulfuric acid to form hydroximinoglutaric ester and in connection with the subsequent reduction by the methods of McIlwain and Hamlin, resulting in low yields or requiring special apparatus. It was therefore a matter of interest to synthesize this amino acid from α-acetoglutaric ester by the relatively simple method of one of us — the synthesis through the stage of the readily accessible arylhydrazones of α-keto acids which enables the above difficulties to be avoided.

On submitting the o-tolylhydrazone of α-ketoglutaric acid * to reduction with zinc dust and acetic acid, we did indeed obtain glutamic acid with a yield at this stage of 81-87%. The synthesis stages may be represented by the following scheme: (see page 888).

The accessibility of the starting material (I), the high yield of the intermediate o-tolylhydrazone (II) which did not require purification, the simplicity of isolation of the free amino acid (III) from the reaction mixture and its formation in high yield are advantages of this method of synthesis of glutamic acid.

* The o-tolylhydrazone had a series of advantages over the phenylhydrazone from the preparative angle.



(I) (II) (III)

EXPERIMENTAL

D,L-Glutamic acid (III). A solution of 5.0 g of the o-tolylhydrazone of α-ketoglutaric acid (m.p. 159-160°) [18], in 50 ml. conc. acetic acid was placed in a long-necked 200 ml round-bottomed flask and heated on a boiling water bath, to this solution was added zinc dust (16 g) in small portions, each portion being dissolved before the next was added. after a period of 20-30 minutes from the start of heating, a total of 50 ml water was introduced in small portions over a period of 1½ - 2 hours. Reduction by heating on the water bath required a period of about 4 hours (negative Bülow reaction). The solution was filtered and the zinc dust on the filter was repeatedly washed with hot water; the filtrate was diluted with water and extracted several times with ether to eliminate the o-toluidine. Zinc ion was precipitated with hydrogen sulfide, the precipitate of zinc sulfide was repeatedly washed on the filter with hot water, and the filtrate and the wash waters evaporated to dryness on a water bath in vacuum. The residue was a thick, light-brown mass which crystallized when stirred with a small quantity of absolute alcohol; the crystals of glutamic acid were drained at the pump, washed with absolute alcohol and dried; weight 2.38-2.55 g; yield 81-87%; m.p. 185-189° with decomposition. Recrystallization from 70% alcohol gave D,L-glutamic acid in the form of colorless, rhombic or hexagonal tablets melting at 195-196° (uncor.) with decomposition. Literature data: 197° [17], 198° [4].

Found %: N 9.76, 9.76. $C_5H_9O_4N$. Calculated %: N 9.52.

SUMMARY

The possibility was shown of extending V. V. Feofilaktov's method for preparation of α-aminocarboxylic acids to α-aminodicarboxylic acids.

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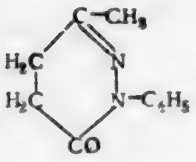
XVI. 1-ARYL-PYRIDAZONE-3-CARBOXYLIC ACIDS AND PRODUCTS OF THEIR TRANSFORMATION

V. V. Feofilaktov and N. K. Semenova

Pyridazone and its derivatives have been relatively little investigated. Their discovery and initial investigation were associated with the clarification of the chemical nature and transformations of hydrazones of ketocarboxylic acids and pyrazolones. Thus, E. Fischer discovered the ability of levulinic acid phenylhydrazone to lose water with formation of a new compound (I) which he called the anhydride of levulinic acid phenylhydrazone [1].



(I)

A little later [2,3] a number of transformations of this compound was studied.

The chemical nature of this anhydride was finally established by investigations [4,5] undertaken in connection with the study of pyrazolones. It was established that reaction of esters of β-ketocarboxylic acids with hydrazine and its derivatives leads to pyrazolone derivatives; in the case, however, of γ-keto acids and their derivatives, such a reaction leads to formation of six-membered nitrogen heterocycles in the shape of pyridazone derivatives [4]. Thus for example the product of condensation of hydrazine hydrate with benzoylacetic ester is pyrazolone, while that with the ester of β-benzoylpropionic acid is pyridazone.

Condensation of other γ-ketocarboxylic acids and their esters [4] gave respectively carboxy- and carbethoxypyridazone derivatives and products of their transformation and pyridazone itself.

On the basis of a study of the behavior of benzopyridazones on alkylation and acetylation, the conclusion was reached [5,6] that tautomerism between the CO and NH groups existed in the pyridazones. Unlike pyrazolones, however pyridazones do not enter into the azo-coupling reaction.

In general, these two groups of compounds differ markedly from each other also in respect to other chemical properties. Thus, pyrazolone derivatives are known to be stable to acids and alkalies but decompose when distilled pyridazone derivatives, in contrast are modified by acids and alkalies and distil without decomposition.

When 1-phenylpyridazone-3-carboxylic acid was subjected to the action of an alcoholic solution of hydrogen chloride, it did not give the expected ester of this acid since the pyridazone ring was ruptured and reclosure to the pyrrole ring took place with formation of an indole derivative – the ethyl ester of 2-carbethoxyindolyl-3-acetic acid [7].

Wolff observed rupture of the pyridazone ring in an alkaline medium. On subjecting 3-methylpyridazone to the action of sodium ethylate, he obtained valeric acid [8].

Pyridazones differ from pyrazolones in being relatively easily oxidized, and advantage was taken of this property in the synthesis of derivatives of phenylpyridazone, phthalazine [9] and pyridazine [10].

In recent years no systematic study has been made of the pyridazones. The literature contains only isolated references to new representatives of this class which were prepared mainly for the purpose of identification of derivatives of γ-ketocarboxylic acids [11, 12, 13] or of substituted hydrazines [14, 15].

Interest in pyridazone derivatives has recently increased somewhat due to their application to the synthesis of sulfanilamide derivatives of pyridazone and pyridazine [15] which exhibit a high bacteriostatic activity and possess chemotherapeutic interest. Thus, for example, 6-sulfanilamido-3-methylpyridazine, prepared from 3-methylpyridazone manifested a higher bacteriostatic activity than sulfathiazole [16].

In our opinion, one of the causes of the neglect of the study of these interesting pyridazone derivatives is the absence of a simple method for their preparation. The only known method of synthesis starts from hydrazones and difficultly accessible keto acids. No attempts had been made to replace the latter by more accessible starting materials.

Bearing in mind the similarity in the methods of preparation of pyrazolones and pyridazones and starting from the ability (discovered and investigated by one of us) of acetosuccinic ester to couple with aryldiazoniums to directly give pyrazolone derivatives [17], we decided to investigate the applicability of this reaction to the preparation of pyridazone derivatives; for this purpose α-acetosuccinic ester was replaced by α-acetoglutaric ester.

We used various aryldiazoniums in the azo-coupling reaction. However, as we had previously observed [18], pyridazone derivatives are not directly formed in the process of azo-coupling, and the coupling products are azo esters or arylhydrazones of esters of α-ketoglutaric acid, saponification of which yields the corresponding arylhydrazones of α-ketoglutaric acid.

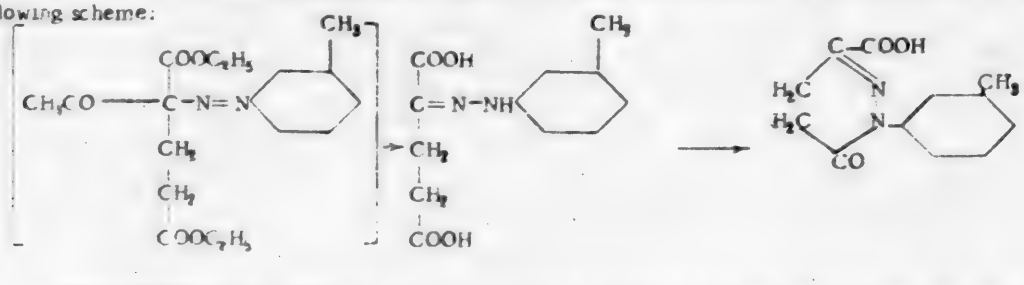
An attempt was therefore made to prepare pyridazones from the separated arylhydrazones. On investigating the ability of these arylhydrazones to undergo ring-closure to pyridazones, it was established that even when subjected to the action of acids (dilute sulfuric, hydrochloric, acetic) or acetic anhydride or when heated, they showed little tendency to be transformed into pyridazone derivatives.

Thus, out of twelve arylhydrazones of α-ketoglutaric acid [18] only two (phenyl- and m-tolylhydrazones) could be cyclized to pyridazones by heating with dilute acids.

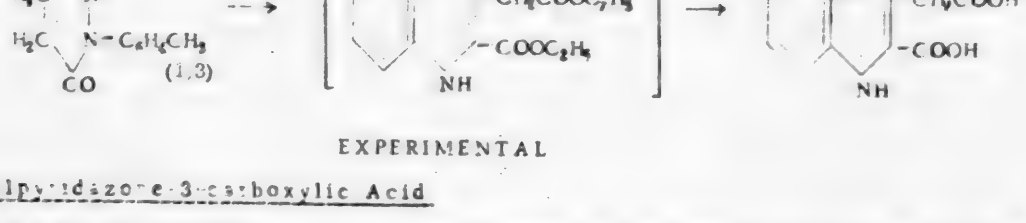
The ability of the m-tolylhydrazone to transform into 1-(m-tolyl)-pyridazone-3-carboxylic acid is apparently due to the CH_3 group – with a weak o,p-orienting effect – being in the m-position to the =N–NH– group and not exerting any appreciable influence on the latter, in consequence of which the latter behaves like the =N–NH– group of an unsubstituted phenylhydrazone.

It should be noted that the γ-phenyl- and γ-m-tolylhydrazones of β-pyruvyl-propionic acid, unlike the phenyl- and m-tolylhydrazones of α-ketoglutaric acid, do not undergo cyclization to pyridazones in spite of the similarity of their structures. It is possible that this is bound up with participation of the hydrogen of the –NH-group in the formation of a hydrogen bond at the carbonyl of the acetyl group which hinders its participation in the cleavage of water, i.e. in the closure of the pyridazone ring.

A study of two of the pyridazone derivatives that we prepared revealed that one of them was identical with the 1-phenylpyridazone-3-carboxylic acid previously described by Wislicenus [7]. We could not find a description of the second derivative – 1-(m-tolyl)-pyridazone-3-carboxylic acid – in the literature. Its formation may be represented by the following scheme:



1-Phenylpyridazone-3-carboxylic acid was reduced to glutamic acid and reconverted into the original phenylhydrazone of α-ketoglutaric acid. Both of the pyridazone-carboxylic acids were transformed into the corresponding indole derivatives.



EXPERIMENTAL

1-Phenylpyridazone-3-carboxylic Acid

0.36 g α-ketoglutaric acid phenylhydrazone (m.p. 152-153°) [18] was heated on a gauze with 40 ml 3% hydrochloric acid until completely dissolved (10-15 minutes). The cooled solution deposited lustrous, slightly pink crystals of 1-phenylpyridazone-3-carboxylic acid in the amount of 2.0 g (91.7%), melting at 169-170°. After recrystallization from water (with addition of carbon), the colorless, lamellar crystals melted at 172°.

Found %: N 12.70, 12.65. $C_{11}H_8O_3N_2$. Calculated %: N 12.84.

Literature data [7]: m.p. 172°.

For the purpose of hydrolysis, 2.18 g 1-phenylpyridazone-3-carboxylic acid was dissolved in 40 ml 10% NaOH and boiled on a gauze for 3-5 minutes. The cooled solution was diluted with water and carefully acidified with conc. hydrochloric acid. The precipitated crystals, consisting of the original phenylhydrazone of α-ketoglutaric acid, weighed 2.32 g (98.6 %) after drying and melted at 152-153° (from alcohol); the composition of the phenylhydrazone was confirmed by a mixed melting test and by determination of the equivalent. Found equiv. 119; 120. $C_{11}H_{12}O_4N_2$. Calculated equiv. 118.

Reduction of 2.18 g 1-phenylpyridazone-3-carboxylic acid with zinc dust and acetic acid in the conditions described in the preceding communication [20] gave D, L-glutamic acid: 0.33 g, i.e. 22%.

For conversion into the indole derivative, 1-phenylpyridazone-3-carboxylic acid and 5 times the amount of absolute ethyl alcohol were refluxed in a flask on a water bath; dry hydrogen chloride was led in through the condenser. Heating was accompanied by deposition of crystals of ammonium chloride on the sides of the flask and was continued for 30 minutes. On cooling, the liquid was poured on to ice-water mixture. The resultant colorless crystals were separated, washed with water and dried. After recrystallization from aqueous ethyl alcohol, the ethyl ester of 2-carbethoxyindolyl-3-acetic acid melted at 85-86° in agreement with the literature [7, 19]; yield quantitative.

A mixed sample with the preparation obtained from α-ketoglutaric acid phenylhydrazone did not give a depression.

Found %: N 4.91, 4.82. $C_{18}H_{21}O_4N$. Calculated %: N 5.09.

1-(m-Tolyl)-pyridazone-3-carboxylic Acid

2.5 g α-Ketoglutaric acid m-tolylhydrazone (m.p. 149°) was digested with 40 ml 5% aqueous sulfuric acid until dissolved. The solution was filtered hot; on cooling with ice, colorless crystals (2.14 g or 92.2%) were deposited; m.p. 146-147°. The crystals did not give a Bulow reaction and had excellent solubility in ethyl and methyl alcohols, ethyl acetate, ether and hot water. After two recrystallizations from aqueous ethyl alcohol, the colorless, lustrous needles of 1-(m-tolyl)-pyridazone-3-carboxylic acid melted at 152°.

Found %: N 12.08, 12.24; equiv. 231, 229. $C_{12}H_{10}O_3N_2$. Calculated %: N 12.07; equiv. 232.

A mixed test with the preparation from the diethyl ester of α-carbethoxyglutaric acid and m-toluidine [18] did not give a melting point depression.

4-Methyl-2-carboxyindolyl-3-acetic Acid

2.32 g 1-(m-tolyl)-pyridazone-3-carboxylic acid (m.p. 152°) and 10 ml 10% alcoholic solution of sulfuric acid were refluxed on a water bath. Two hours after the commencement of heating, there was appreciable separation of ammonium sulfate crystals; heating was continued for 8 hours.

The reaction mixture — a light-brown liquid — was poured into water which contained ice; the resultant viscous oil was separated from the alcoholic liquid by decantation and saponified with 10% alcoholic-aqueous solution of NaOH. Acidification of the aqueous solution of the salt caused greyish crystals of acid to separate in the amount of 1.97 g (84.4%). The substance is readily soluble in acetone, ethyl acetate, ether, methyl and ethyl alcohols and glacial acetic acid; very sparingly soluble in benzene.

After recrystallization from aqueous ethyl alcohol with addition of carbon, 4-methyl-2-carboxyindolyl-3-acetic acid formed colorless crystals which melted at 186° with decomposition.

Found %: N 5.93, 5.78; equiv., 109, 113. $C_{12}H_{11}O_4N$. Calculated %: N 6.00; equiv. 116.5.

SUMMARY

1. It was established that arylhydrazones of α-ketoglutaric acid and arylhydrazones of β-pyruvylpropionic acid do not spontaneously cyclize to the pyridazone ring.

2. Arylhydrazones of α-ketoglutaric acid differ in respect of ease of cyclization into pyridazone derivatives. It was only possible to cyclize the phenyl- and m-tolylhydrazones.

3. γ-Arylhydrazones of β-pyruvylpropionic acid generally do not cyclize to pyridazone derivatives in the conditions investigated.

4. The possibility is demonstrated of reduction of 1-phenylpyridazone-3-carboxylic acid into D,L-glutamic acid.

4. The possibility is demonstrated of reduction of 1-phenylpyridazone-3-carboxylic acid into D,L-glutamic acid and of transformation into the original α-ketoglutaric acid phenylhydrazone, and of transformation into 2-carboxyindolyl-3-acetic acid in quantitative yield.

5. 1-(m-Tolyl)-pyridazone 3-carboxylic acid was also transformed into 4-methyl-2-carboxyindolyl-3-acetic acid in high yield.

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* See Consultants Bureau English translation, page 463 ff.
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N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR TRANSFORMATION INTO HETEROCYCLIC COMPOUNDS

XX. REGULARITIES OF INTRAMOLECULAR CYCLIZATION IN ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS

P. A. Petyunin and V. S. Shklyaev

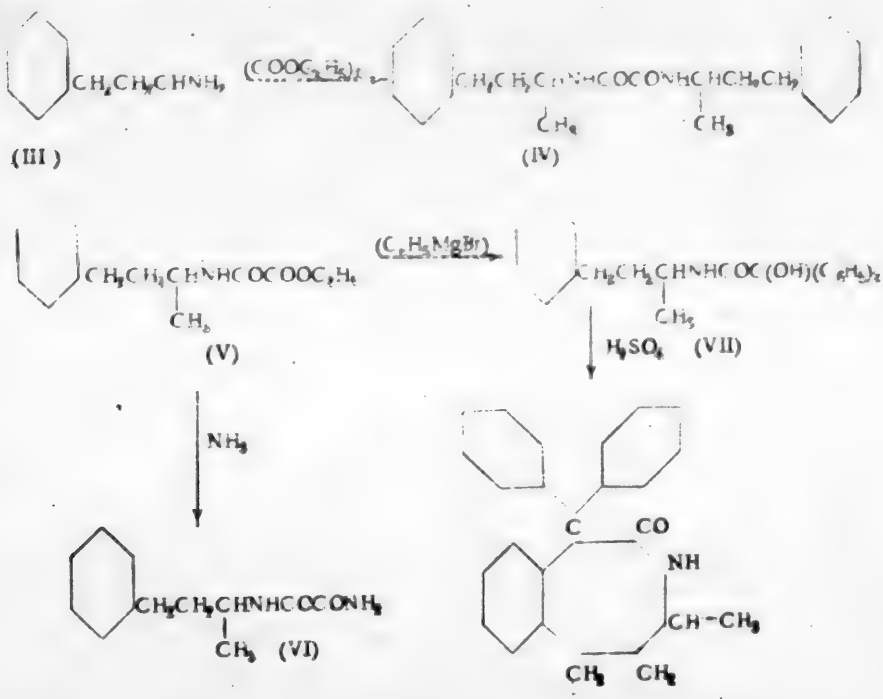
Many investigations have been devoted to the problem of formation of cyclic systems from open-chain compounds. At the present time the ideas of Mohr [1] and Ruzicka [2] are generally accepted. These authors consider that ring closure is determined by two factors acting simultaneously: the strain in the formed ring and the distance between the reacting groups. Isolation of the molecule, as one of the conditions of cyclization, may be achieved by using dilute solutions in high vacuum [3]. These concepts, however, do not cover all the diverse causes influencing the process of ring formation. N. A. Domnin [4] points out that with a minimum of six, if not five, members in the ring, the reluctance to cyclize is due not to strain but to other factors such as spatial separation of the end reactive groups. There are probably other causes (still unknown). Study of the regularities of formation of ring systems from open-ring compounds have been made for the most part with carbon rings.

According to very recent experimental data, the valence angles of trivalent nitrogen and of oxygen in organic compounds only differ slightly from the angles of a regular tetrahedron [5]. Consequently the process of ring formation ought to be studied to an equal extent with reference to heterocycles. We decided to study the regularities of formation of ring systems during intramolecular condensation of aryl amides of hydroxy carboxylic acids. In previous investigations it had been established that intramolecular ring closure is possible in aryl amides of two types of hydroxy-carboxylic acids:

$ArNHCO(CH_2)_nC(OH)Ar_2$ (I) and $Ar(CH_2)_nNHCOC(OH)Ar_2$ (II).

Compound (I), when n = 0 or 1, forms 5- or 6-membered rings, respectively. When n = 2, the hetero-ring does not close and saponification occurs with formation of an aromatic amine and a γ-hydroxy carboxylic acid [6]. Compounds (II) are more useful because their structure imparts exceptional resistance to saponification [6]. Successful condensations of this type were performed with n = 0, 1 and 2 [7].

We set ourselves the objective of performing the reaction for n = 3 and of forming an 8-membered ring. The latter was synthesized by the following scheme:



Heating of 1-phenyl-3-aminobutane (III) with ethyl oxalate gave two compounds: the di-(1-phenyl-3-butylamide) of oxalic acid (IV) and the ethyl ester of 1-phenyl-3-butyloxamic acid (V) (expt. 1). The latter was converted into the amide (VI) (expt 2). Treatment of (V) with phenyl magnesium bromide gave the 1-phenyl-3-butylamide of benzilic acid (VII), which underwent intramolecular condensation to the lactam of 2-(γ-aminobutyl)-triphenylacetic acid (VIII) (expt. 4).

To clarify the problem of our investigation, the starting substances taken were compounds of the type of $Ar'CH_{2n}NHCOC(OH)Ar'_2$, where n = 0, 1, 2 and 3; Ar' = C_6H_5–, p-$CH_3C_6H_4$– and p-$CH_3OC_6H_4$–. A new series of compounds was prepared in this way (expts. 5, 6, 7). The velocity of ring closure in these was determined by the procedure described in detail in the preceding communication.

The relation between the velocity of ring closure and the distance separating the reacting groups was clarified with reference to the formation of 5-, 6-, 7- and 8-membered rings. The data obtained are set forth in Table 1 (aryl amides nos 1, 2, 3 and 4). The reactivity of the carbonyl carbon atom in these aryl amides was substantially identical since it is governed by the nature of the radical attached to them. These compounds have the same basicity (they form hydrobromic salts with 88% H_2SO_4, and their transformation into heterocyclic compounds requires an identical amount of sulfuric acid). Consequently, the differences in the speeds of ring closure may be explained by the spatial separation of the end reactive groups.

We see from the data that with increasing distance between the end reactive groups, the speed of ring closure decreases in the order: 5>6>7>8, i.e. a reciprocal dependence exists between the speed of closure of a ring and its size. This conclusion is fully consistent with the literature data for polymethylene rings [8] and cyclic imines [9]. On comparing these data, however, with the velocity of ring closure in p-tolylic acid anilide (aryl amide No. 5), we see that the stated relation between size of ring and ease of cyclization is far from possessing general validity. Thus, the 5-membered heterocycle in aryl amide no. 5 closes 27 times slower than the 6-membered ring (aryl amide no 2), 20 times slower than the 7-membered ring (aryl amide no. 3), and 5 times slower than the 8-membered ring (aryl amide no. 4).

TABLE 1

Velocity of Closure of 5-, 6-, 7- and 8-Membered Rings in Aryl Amides of α-Hydroxycarboxylic Acids*

Prep No.	Formula	Amount of H_2SO_4 (ml)	Velocity of closure of ring at 20°	Size of ring
1	$C_6H_5NHCOC(OH)(C_6H_5)_2$	5	400	5
2	$C_6H_5CH(CH_3)NHCOC(OH)(C_6H_5)_2$	5	328	6
3	$C_6H_5CH_2CH_2NHCOC(OH)(C_6H_5)_2$	5	240	7
4	$C_6H_5CH_2CH_2CH(CH_3)NHCOC(OH)(C_6H_5)_2$ . .	5	60	8
5	$C_6H_5NHCOC(OH)(C_6H_4CH_3\ p)_2$	1.5	12	5

The high velocity of formation of 6-, 7- and 8-membered ring systems in aryl amides of benzilic acid in comparison with the 5-membered ring of p-tolylic acid anilide can no longer be explained by the spatial separation of the end groups as the sole factor influencing the formation of ring systems which are strain free. On the other hand, this anomaly can be readily explained by the differing reactivities of the end groups. As we know, the reactivity of the carbonyl carbon is reduced in the anilide of p-tolylic acid, in comparison with the aryl amides of benzilic acid, under the influence of the electron donating methyl groups. Consequently, the speed of ring closure is considerably reduced [10]. This signifies that, apart from the distance between the reacting groups, the reactivity of the groups themselves is a factor in the formation of cyclic systems.

On the basis of the literature data, we may infer that the reactivity of the end groups may profoundly influence the case of formation of cyclic systems. Ruzicka [11] observes, for example, that maximum yields of cyclic ketones from salts of dicarboxylic acids can be attained by using thorium salts but not calcium salts. According to Ziegler [12]

* Experiments were performed with 0.015 mol. solutions of aryl amides in 1 liter glacial acetic acid. 1 ml of this solution was used in an experiment. The speed of ring closure is expressed in relative numbers. The unit was taken as the velocity of closure of the 5-membered ring of the o-anisidide of 4,4'-dimethoxybenzilic acid which was 300 minutes

replacement of lithium by potassium improves the reaction results in the cyclization of dicarboxylic acid nitriles. Freundlich and Salomon [9] established that the introduction of a phenyl group in the α-position of a ω-haloalkylamine increases the reaction velocity more than 1000 times. There are, however, no studies in the literature of a comprehensive character on the relation between reactivity of end groups and formation of cyclic systems. This fact becomes understandable when we bear in mind that in the compounds used by the cited authors for formation of rings, the reactivity of the groups varied within narrow limits.

The distance factor has the greatest influence on cyclization when the reactivity of the end groups is reduced. Thus, for example, in aryl amides of p-tolylic acid (Table 2) the 5-membered ring closes 3.1 times as fast as the 6-membered ring while in aryl amides of benzilic acid (aryl amides 1 and 2, Table 1), whose end groups are more reactive, the 5-membered ring is formed 1.2 times as fast as the 6-membered ring.

TABLE 2

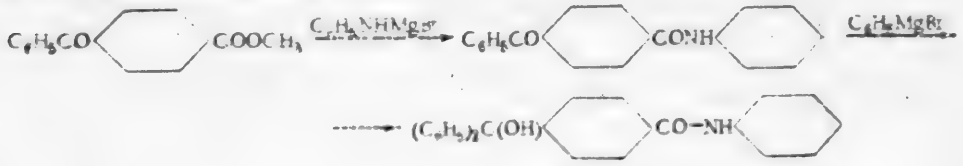
Velocity of Closure of 5- and 6-Membered Rings in Aryl Amides of p-Tolylic Acid

Prep. No.	Formula	Amount of H_2SO_4 (ml)	Velocity of closure of ring at 30°	Size of ring
1	$C_6H_5NHCOC(OH)(C_6H_4CH_3\text{-}p)_2$	1.5	43	5
2	$C_6H_5CH(CH_3)NHCOC(OH)(C_6H_4CH_3\text{-}p)_2$	1.5	13.6	6

In the course of this research it was a matter of interest to study ring closure in the compounds $Ar(CH_2)_nNHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$, where n = 0, 1, 2, because they contain less reactive groups than aryl amides of p-tolylic acid. From the data of Table 3 we see that ring closure is very slow in the 5-membered heterocycle (aryl amide no. 1) while aryl amides 2 and 3 are generally not transformed into cyclic compounds (expt. 8).

In connection with the effect of the terminal reactive groups on ring closure, we must revise our ideas about the limits of condensation in the sense of the magnitude of the formed ring. Experiments have shown that in compounds $Ar(CH_2)_nNHCOC(OH)(C_6H_5)_2$ condensation is possible when n = 3 with formation of an 8-membered ring, whereas in the compounds $Ar(CH_2)_nNHCOC(OH)(C_6H_4OCH_3\text{-}p)_2$ condensation only proceeds when n = 0 with formation of a 5-membered ring. Consequently the limits of cyclization of aryl amides of α-hydroxy carboxylic acids may be broadened by introducing electron-accepting groups into the phenyl radicals at the carbonyl carbon atom, and the limits may be narrowed by introducing electron-donating substituents.

Ring closure is of theoretical interest in the case of aryl amides in which a strain factor is involved apart from the distance factor. From this standpoint we synthesized the anilide of p-triphenylcarbinol carboxylic acid (IX) according to the scheme below (expts. 9 and 10)



(IX)

We unsuccessfully attempted to realize the intramolecular closure of the heterocycle in (IX) (expt. 11). Inspection of the formula of molecule (IX) indicated that an exceptionally large deformation of the valence angles of the carbon atoms would be required for approach of the carbonyl carbon to the o- or p-position of the aryl amide residue to a distance equal to the length of the covalent bond.

A problem that inevitably arises in the study of cyclic systems relates to the reactions competing with ring formation. Reactions of formation of monomeric ring systems are known to be accompanied by the formation of polymeric compounds [13].

Repeated experiments on condensation of aryl amides of hydroxy carboxylic acids established that the reactions give high yields of only monomeric cyclic systems. The absence of products of intermolecular reaction is due to the intramolecular ring closure in aryl amides of hydroxy carboxylic acids proceeding via cation of a halochromic salt. In this connection not only are intermolecular reaction between ions of identical charge hindered but also their close approach.

Hence for organic compounds capable of ring closure by an ionic mechanism, neither dilution nor a vacuum is necessary for isolation of the molecule, since the presence of a charge definitely ensures isolation.

TABLE 3

Prep. No.	Formula	Amount of H_2SO_4 (ml)	Velocity of ring closure at 20°	Size of ring
1	o-$CH_3OC_6H_4NHCOC(OH)(C_6H_4OCH_3$-p$)_2$.	0.1	1	5
2	$C_6H_5CHNHCOC(OH)(C_6H_4OCH_3$-p$)_2$ . . . . CH_3	0.1	Does not cyclize	6
3	$C_6H_5CH_2CH_2NHCOC(OH)(C_6H_4OCH_3$-p$)_2$.	0.1	Does not cyclize	7

We unsuccessfully attempted to realize the intermolecular reaction of aryl amides with phenols according to the following scheme:

$$ArNHCOC(OH)Ar_2 + C_6H_5OH \rightarrow H_2O + Ar\text{-}NHCOC(C_6H_4OH)Ar_2.$$

The idea behind these experiments was that the benzene nucleus in phenols is more nucleophilic than in acylated aromatic amines. The experiments were performed in presence of anhydrous tin chloride between the anilide or α-naphthalide of benzilic acid and the p-phenetidide of 4,4'-dimethoxybenzilic acid on the one hand with phenol and resorcinol on the other hand (expts. 12, 13 and 14). In this case also, condensation proceeds with formation of monomeric cyclic systems. The data that we obtained indicate that intermolecular reaction will be more probable with those aryl amides whose intramolecular ring closure is hindered by the great distance between their end groups.

EXPERIMENTAL

Di-(1-phenyl-3-butylamide) of oxalic acid and the ethyl ester of 1-phenyl-3-butyl-oxamic acid (expt. 1). To a solution of 16 g 1-phenyl-3-aminobutane • in 20 ml alcohol was added 20 g ethyl oxalate. At the close of the reaction the mass was heated on the water bath until it gave a neutral reaction to litmus. Di-(1-phenyl-3-butylamide) of oxalic acid came down on cooling. It was filtered off and recrystallized from alcohol. Colorless needles, m.p. 170-172°, insoluble in water, soluble on heating in alcohol, benzene and toluene. Yield 0.5 g or 2.6 % of the theoretical calculated on the 1-phenyl-3-aminobutane taken.

0.0358 g substance: 19.7 ml 0.01 N H_2SO_4. 0.0390 g substance: 21.1 ml 0.01 N H_2SO_4. Found %: N 7.72, 7.61. $C_{22}H_{28}O_2N_2$. Calculated %: N 7.96.

The main product of the reaction was separated from the alcoholic filtrate. After removal of the solvent, the residue was distilled in vacuum to give a colorless, oily liquid with b.p. 183.5-185° (4 mm). Yield 23.5 g or 51% of the theoretical.

d_4^{18} 1.0821, n_D^{18} 1.5135; MR_D 69.21; calculated 68.52.

0.0228 g substance: 8.9 ml 0.01 N H_2SO_4. 0.0208 g substance: 8.1 ml 0.01 N H_2SO_4. Found %: N 5.47, 5.45. $C_{14}H_{19}O_3N$. Calculated %: N 5.62.

Amide of 1-phenyl-3-butyloxamic acid (expt. 2). Gaseous ammonia was passed into a cooled alcoholic solution of 1 g ethyl ester of 1-phenyl-3-butyloxamic acid. The precipitate was filtered and crystallized from alcohol. Slender, colorless needles with m.p. 180°. Yield 0.8 g or 91% of the theoretical.

The amide is insoluble in water, readily soluble in hot alcohol, benzene and toluene.

0.0166 g substance: 11.4 ml 0.01 N H_2SO_4. 0.0146 g substance: 14 ml 0.01 N H_2SO_4. Found %: N 13.32, 13.41. $C_{12}H_{16}O_2N_2$. Calculated %: N 12.72.

1-Phenyl-3-butylamide of benzilic acid (expt. 3). To the phenyl magnesium bromide prepared from 15.7 g (0.1 mole) bromobenzene and 2.3 g (0.1 mole) magnesium in 50 ml ether was added a solution of 5 g (0.02 mole) ethyl ester of 1-phenyl-3-butyloxamic acid. The reaction product was recrystallized from 100 ml 70% alcohol. Colorless needles with m.p. 83°. The compound is sparingly soluble in gasoline, easily soluble in other organic solvents. With concentrated sulfuric acid it gives a brown coloration which changes to green and then to weak yellow. Yield 4 g or 55.5% of the theoretical.

• 1-Phenyl-3-aminobutane was prepared by the Leuckhardt reaction from benzylacetone and ammonium formate in 56% yield. B.p. 100° (12 mm). Literature: 101-102° (14 mm) [14].

0.1066 g substance: 4.5 ml 0.01 N H_2SO_4. 0.0304 g substance: 7.6 ml 0.01 N H_2SO_4. Found %: N 3.8, 3.5. $C_{24}H_{23}O_2N$. Calculated %: N [illegible].9.

Lactam of 2-(γ-aminobutyl) triphenylacetic acid (expt. 4). Starting substances: a solution of 1 g 1-phenyl-3-butylamide of benzilic acid in 6.5 ml glacial acetic acid and 17 ml conc. sulfuric acid. A brown color was first developed and changed gradually to green. Toward the end of the reaction the solution acquires a yellow-orange color. The reaction mass was poured into 50 ml water and the resultant precipitate was worked up in the usual manner. Crystallization from glacial acetic acid gave a fine crystalline powder with m.p. 153°. Readily soluble in alcohol and acetic acid, more difficultly soluble in benzene and toluene. Yield 0.5 g or 52% of the theoretical.

0.0366 g substance: 10 ml 0.01 N H_2SO_4. 0.0177 g substance: 5.2 ml 0.01 N H_2SO_4. 0.0094 g substance: 0.1028 g camphor: Δt 11.2°. 0.0120 g substance; 0.1240 g camphor: Δt 11.5°. Found %: N 3.82, 4.11; M 326.6, 336.6. $C_{24}H_{23}ON$. Calculated %: N 4.11; M 341.

α-Phenylethylamide of p-tolylic acid (expt. 5). Materials: 6.6 g (0.03 mole) ethyl ester of α-phenylethyl-oxamic acid, 26.16 g (0.12 mole) p-iodotoluene and 2.76 g (0.12 mole) magnesium. The reaction product slowly crystallizes from benzene in the form of colorless plates with m.p. 112°. Readily soluble in the common organic solvents. With conc. sulfuric acid it forms a transient red color. Yield 1.5 g or 13.7% of the theoretical.

0.0356 g substance: 10.7 ml 0.01 N H_2SO_4. 0.0348 g substance: 9.7 ml 0.01 N H_2SO_4. Found %: N 4.21, 3.9. $C_{24}H_{23}O_2N$. Calculated %: N 3.9.

α-Phenylethylamide of 4,4'-dimethoxybenzilic acid (expt. 6). The reaction was performed between 6.63 g (0.03 mole) ethyl ester of α-phenylethyloxamic acid and p-anisyl magnesium iodide prepared from 28 g (0.12 mole) p-iodoanisole and 2.91 g (0.12 mole) magnesium in 120 ml ether. After decomposition of the reaction mass and distillation of the volatile products with steam, there remained a brown substance with an oily consistency. This was dissolved in alcohol. After standing for 24 hours, the solution deposited colorless long needles with m.p. 96°. Yield 2.6 g or 22% of the theoretical. Insoluble in water and readily soluble in common organic solvents. With conc. sulfuric acid it forms a stable crimson coloration.

0.0230 g substance: 5.8 ml 0.01 N H_2SO_4. 0.0250 g substance: 6.7 ml 0.01 N H_2SO_4. Found %: N 3.53, 3.74. $C_{24}H_{23}O_4N$. Calculated %: N 3.58.

β-Phenylethylamide of 4,4'-dimethoxybenzilic acid (expt. 7). Starting materials: 5 g (0.023 mole) ethyl ester of β-phenylethyloxamic acid, 26.5 g (0.113 mole) p-iodoanisole and 2.7 g (0.113 mole) magnesium. Crystallizes slowly from alcohol in long needles, m.p. 107-108°. Yield 3.8 g or 43% of the theoretical. Insoluble in water and readily soluble in organic solvents. With conc. sulfuric acid it forms a stable crimson coloration.

0.0272 g substance: 7.3 ml 0.01 N H_2SO_4. 0.0494 g substance: 12.4 ml 0.01 N H_2SO_4. Found %: N 3.75, 3.52. $C_{24}H_{23}O_4N$. Calculated %: N 3.58

Attempt to form a heterocycle from α- and β-phenylethylamides of 4,4'-dimethoxybenzilic acid (expt. 8). Experiments were performed in identical conditions. We describe an experiment with α-phenylethylamide of 4,4'-dimethoxybenzilic acid. To a solution of 0.5 g α-phenylethylamide of 4,4'-dimethoxybenzilic acid in 5 ml glacial acetic acid was added 0.1 ml conc. sulfuric acid. The resultant crimson coloration did not disappear after standing for 120 hours. After this the reaction mixture was heated for 3 hours on the water bath. The solution, which did not lose its color even after heating, was poured into 20 ml water. Yield 0.4 g air dry substance, equivalent to 80% of the amount of α-phenylethylamide of 4,4'-dimethoxybenzilic acid taken for the reaction. Needles (from alcohol), m.p. 94-96°. A mixed sample with an authentic specimen of α-phenylethylamide of 4,4'-dimethoxybenzilic acid did not give a depression of melting point.

In an experiment with the β-phenylethylamide of 4,4'-dimethoxybenzilic acid the same results were obtained: about 80% was recovered unchanged. After recrystallization from alcohol the substance had the melting point of the original product (107-108°) and a mixed melting test with the original substance did not give a depression.

Anilide of p-benzoylbenzoic acid (expt. 9). This was prepared by the Sodoux reaction [15]. To the phenyl magnesium bromide prepared from 5.5 g (0.05 mole) ethyl bromide, 1.5 g magnesium and 5.1 g (0.05 mole) aniline in 30 ml ether was added a solution of 5.5 g (0.02 mole) methyl ester of p-benzoylbenzoic acid in 15 ml ether.

After heating for a short period, the reaction mass was decomposed with 5% hydrochloric acid. Needles (from toluene) with m.p. 163-164°. The literature [16] gives 171°.

Anilide of p-triphenylcarbinol carboxylic acid (expt. 10). Starting materials: 1.7 g (0.0056 mole) p-benzoylbenzoic acid anilide, 5.1 g (0.025 mole) iodobenzene and 0.6 g magnesium. Decomposition of the reaction mass with saturated ammonium chloride solution and removal of the ether left a solid mass which crystallized from alcohol. M.p. 182°. Yield 1.7 g or 80% of the theoretical. The literature [17] reports a m.p. of 182° for the anilide of p-triphenylcarbinol carboxylic acid. With 70% sulfuric acid the anilide forms a yellow coloration; with conc. hydrochloric acid it does not give a coloration.

Found %: N 3.66, 3.52. $C_{26}H_{21}O_2N$. Calculated %: N 3.69.

Attempt to cyclize the anilide of p-triphenylcarbinol carboxylic acid (expt. 11). To an acetic acid solution of 0.2 g anilide of p-triphenylcarbinol carboxylic acid was added 2 ml conc. sulfuric acid. A dark-red color appeared and did not disappear on heating the reaction mass on a water bath for 30 minutes. The product was isolated by the usual procedure. Colorless crystals (from alcohol), m.p. 182°. A mixed sample with the original substance melted without depression.

3,3-Bis-(4-methoxyphenyl)-5-ethoxyoxindole (expt. 12). To a solution of 2 g (0.006 mole) p-phenetidide of 4,4'-dimethoxybenzilic acid and 0.8 g (0.009 mole) phenol in 20 ml benzene was added 2 g (0.008 mole) anhydrous tin chloride. The reaction mass was heated for a brief period on a water bath until the red-violet color had disappeared. After cooling, the contents of the flask were poured into 50 ml water. The benzene layer was separated and evaporated to a small volume on a water bath. A crystalline mass separated on standing. Needles (from alcohol) with m.p. 179-180°, in agreement with the data for the previously described 3,3-bis-(4-methoxyphenyl)-5-ethoxyoxindole [18]. A mixed sample gave no depression. Yield 1.5 g or 78%.

3,3-Diphenyl-6,7-benzooxyindole (expt. 13). Reagents: 1.5 g (0.004 mole) α-naphthalide of benzilic acid, 0.5 g (0.004 mole) resorcinol in 20 ml benzene and 2 g (0.008 mole) anhydrous tin chloride. Yield 1.4 g or 98%. Needles (from alcohol) with m.p. 254°, in agreement with the literature data for 3,3-diphenyl-6,7-benzooxyindole [19]. A mixed melting point test did not give depression.

3,3-Diphenyloxyindole (expt. 14). Reagents: 3 g (0.011 mole) benzilic acid anilide, 1.1 g (0.011 mole) phenol and 3.0 g (0.012 mole) tin chloride. Crystallization from benzene gave small rods with m.p. 225°. These data agree with those for 3,3-diphenyloxyindole [20]. A mixed sample with an authentic specimen melted without depression. Yield 2 g or 75.5%.

SUMMARY

1. Intramolecular condensation was effected of the 1-phenyl-3-butylamide of benzoic acid and the possibility was thereby demonstrated of obtaining 8-membered ring systems by intramolecular condensation of aryl amides of hydroxycarboxylic acids.

2. The velocity of closure of the heterocycle in aryl amides of hydroxy carboxylic acids falls in the order 5>6>7>8, which is consistent with data for carbon rings.

3. In the formation of 5-, 6-, 7- and 8-membered heterocycles in aryl amides of hydroxy carboxylic acids apart from the distance factor, the reactivity of the same end groups enters into play as a factor in the formation of cyclic systems.

The size limitation on intramolecular condensation of aryl amides of hydroxy carboxylic acids depends on the reactivity of the end groups. Introduction of electron-accepting substituents in the phenyl radicals at the carbonyl carbon makes possible the formation of a larger ring than when electron-donating substituents are introduced.

4. The unsuccessful attempt to close the ring in the anilide of p-triphenylcarbinol carboxylic acid is explained by the great strain in formation of the ring.

5. On the basis of data for closure of heterocycles in aryl amides of hydroxy carboxylic acids, it is shown that for organic compounds capable of ring closure by an ionic mechanism, neither dilution nor vacuum is necessary for isolation of the molecules since the presence of a charge suppresses the reaction of intermolecular interaction.

6. Intermolecular reaction does not take place when arylamides of α-hydroxy carboxylic acids are treated with phenols in presence of anhydrous tin chloride, only products of intramolecular reaction are formed.

7. Anhydrous tin chloride can be successfully utilized for the intramolecular closure of heterocycles in aryl amides of α-hydroxy carboxylic acids.

8. A series of previously undescribed acyl amides of α-hydroxy carboxylic acids and heterocyclic and other compounds were prepared and their properties studied.

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•••• See Consultants Bureau English translation, page 2063 ff.

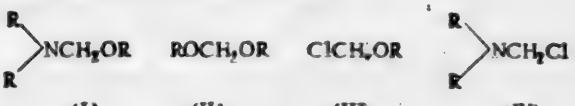
••••• See Consultants Bureau English translation, page 359 ff.

•••••• See Consultants Bureau English translation, page 1977 ff.

REACTION OF ORGANOMAGNESIUM COMPOUNDS WITH DERIVATIVES OF 3,4-DIHYDRO-3-ALKYL-1,3-2-BENZOXAZINES

K. G. Mizuch

The reactivity of compounds containing a methylene group linked to various atoms other than carbon is known to be increased in comparison with similarly structured compounds whose methylene group is linked to identical atoms. As an example we may cite the greater ease of reaction of dialkylaminomethylalkyl ethers (I) with organomagnesium compounds by comparison with compounds of the type of acetals (II) [1]. Examples of compounds whose increased reactivity is caused by the presence of another atomic grouping are α-halomethyl ethers (III) and chloromethylenedialkylamines (IV) [2].

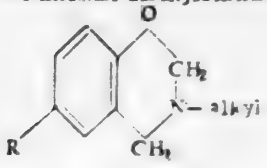


(I) (II) (III) (IV)

As was shown by the author and Ts. M. Gelfer [3], the effect of non-carbon atoms—intensified in some cases by the action of the electrophilic phenyl group—on the methylene group of certain carbonium ethers may be so great as to provoke a more or less complete shifting of the center of electrophilic activity in the ether molecule from the carbonyl carbon to the carbon of the methylene group.

In all the specified types of compounds the atomic groupings [$>NCH_2O-$, $>NCH_2Cl$, $ClCH_2O-$, $BrCH(C_6H_5)O-$], giving rise to an especially easy or uncharacteristic (for these compounds) course of reaction, are partly open chains. It was a matter of interest to investigate the behavior of compounds whose $>NCH_2O-$ grouping was part of a ring.

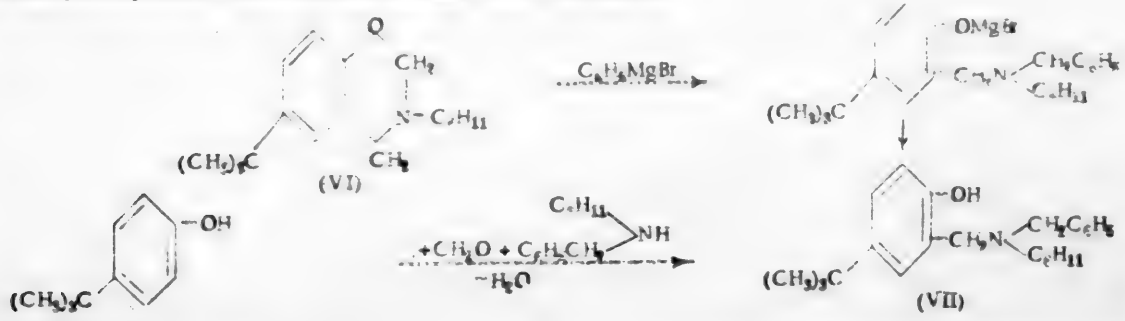
It seemed to us that this problem might be solved by studying the behavior of organomagnesium compounds toward the recently synthesized derivatives of 3,4-dihydro-3-alkyl-1,3,2-benzoxazine (V) [4] which may be regarded as internal dialkylaminomethylphenyl ethers.



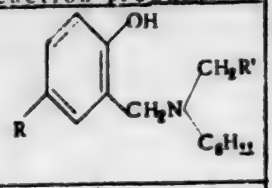
(V)

Due to the presence of the $>NCH_2O-$ grouping in the ring, compounds (V) differ from dialkylaminomethylalkyl ethers in being more stable. Whereas dialkylaminomethylalkyl ethers are cleaved even in the cold by traces of acids to form the original components (secondary amine, alcohol and formaldehyde), compounds (V) are capable of forming hydrochlorides and only lose formaldehyde when heated with acid [4, 5]. It was therefore suggested that the action on (V) of organomagnesium compounds would be accompanied by attack of the nucleophilic radical of the organomagnesium compound on the carbon of the methylene group with consequent ring opening and formation of 2-dialkylaminomethyl derivatives of phenol, although the reaction itself may be expected to be less intensive than in the case of ethers (I).

For the purpose of putting this theory to the test, we reacted phenyl magnesium bromide with 3,4-dihydro-3-cyclohexyl-6-tert. butyl-1,3,2-benzoxazine (VI) and we established that the reaction is energetic and is accompanied by appreciable rise of temperature. After decomposition of the reaction mixture with ammonium chloride, the main reaction product was a substance melting (from ethyl alcohol) at 137-137.5° and differing from the original benzoxazine. The elementary analysis gave the formula $C_{26}H_{37}ON$. The compound contained one active hydrogen atom. This enabled the structure 2-(benzylcyclohexylaminomethyl)-4-tert. butylphenol (VII) to be assigned to it. The structure of (VII) was confirmed by its identification with the substance prepared by known method by direct reaction of N-cyclohexylbenzylamine with formaldehyde and 4-tert. butylphenol.



(VI) (VII)

R'MgX	Reaction product  R	R'	Method of isolation	Yield (%)	Melting point	Formula
CH_3MgI	$(CH_3)_3C$	CH_3	A	82.2	85.4-86•	$C_{19}H_{31}ON$
$(CH_3)_2CHCH_2MgBr$	$(CH_3)_3C$	$(CH_3)_2CHCH_2$	A	79	63.2-64•	$C_{22}H_{37}ON$
$CH_2=CHCH_2MgBr$	$(CH_3)_3C$	$CH_2=CHCH_2$	A	85.5	46.8-47.5•	$C_{21}H_{33}ON$
$C_6H_{11}MgCl$	$(CH_3)_3C$	C_6H_{11}	A	87	101.2-101.8••	$C_{24}H_{39}ON$
C_6H_5MgBr	$(CH_3)_3C$	C_6H_5	B	82.5	137 -137.5•	$C_{24}H_{33}ON$
C_6H_5MgBr	C_6H_5	C_6H_5	B	92.8	117.2-117.8•••	$C_{36}H_{33}ON$
$C_6H_5CH_2MgCl$	$(CH_3)_3C$	$C_6H_5CH_2$	B	93	136.6-137.2••••	$C_{32}H_{35}ON$

Note. Purification: •from ethyl alcohol; ••from methyl alcohol; •••from methyl alcohol-ethyl acetate (2:1);

Attention should be drawn to the fact that Burke and co-workers [5] had treated compounds of type (V) with CH_3MgI for determination of their active hydrogen, but had not observed a reaction with organomagnesium compounds. In a more recent publication [6], which appeared after the completion of the experimental part of the present investigation, Burke and co-workers reported the preparation of 1-dibenzylaminomethyl 2-naphthol in 8% of the theoretical yield by the action of a large excess of C_6H_5MgBr on 2,3-dihydro-2-benzyl-1H-naphth [1.2-e]-m-oxazine. Since our own data gave a clearer idea of the course of the reaction of 3,4-dihydro-3-alkyl-1,3,2-benzoxazines with organomagnesium compounds than could be derived from paper [6], we decided to publish our results.

Our work differed from [6] in that the transformation in question was realized not only with C_6H_5MgBr but also with a series of other organomagnesium compounds. When (VI) was reacted with methyl magnesium iodide, isobutyl magnesium bromide, allyl magnesium bromide, benzyl magnesium chloride and phenyl magnesium bromide, the yields of the isolated pure dialkylaminomethyl derivatives were 79-93% of the theoretical. A benzoxazine with another structure was tested in the shape of 3,4-dihydro-3-cyclohexyl-6-phenyl-1,3,2-benzoxazine•, from which was prepared – by treatment with phenyl magnesium bromide – 2-(benzylcyclohexylaminomethyl)-4-phenylphenol in over 90% yield. These data show beyond doubt that ring-opening with formation of 2-dialkylaminomethyl derivatives of phenol is the main direction of the reaction.

The effect of the sterically hindered organomagnesium compounds was investigated by carrying out the reaction of (VI) with tert. butyl magnesium bromide and cyclohexylmagnesium chloride. Also in this case the reaction proceeded according to the same scheme and the products were 2-(2,2-dimethylpropylcyclohexylaminomethyl)-4-tert. butylphenol and 2-(cyclohexylhexahydrobenzylaminomethyl)-4-tert. butylphenol.

Special interest is attached to the preparation of 2-dialkylaminomethyl derivatives of phenols by the action of organomagnesium compounds on derivatives of 3,4-dihydro-3-alkyl-1,3,2-benzoxazine in connection with recent studies of this type of compound as therapeutic agents [7]. By the classical method of preparation of 2-dialkylaminomethyl derivatives of phenols containing various substituents at the nitrogen, it is necessary to start from formaldehyde and the appropriate secondary amines whose synthesis involves well known difficulties and gives low yields [8]. The reaction utilizing derivatives of 3,4-dihydro-3-alkyl-1,3,2-benzoxazines and organomagnesium compounds enables the preparation of 2-dialkylaminomethyl derivatives of phenols with high yields and wide diversification of the substituents in the resultant N-dialkylaminomethyl group.

EXPERIMENTAL

Reaction of (V) with organomagnesium compounds was performed in an ethereal medium by addition, with stirring, of the crystalline benzoxazine to an excess of organomagnesium compound freed from residues of magnesium. The amount of organomagnesium compound varied in individual experiments from 2 to 4 moles per mole of benzoxazine. During the addition of the benzoxazine the temperature of the reaction mass was maintained in the range of −5° to +5°. Thereupon the mixture was heated a short period at the boiling point of ether. Reaction products were isolated by two procedures. When the reaction product was soluble in ether it was extracted after decomposition of

• Formula (V) where alkyl = cyclo-C_6H_{11}, R = C_6H_5

Calculated (%)			Found (%)		
C	H	N	C	H	N
78.84	10.80	4.84	78.71	10.73	4.84
79.70	11.25	4.22	79.78	11.25	4.40
79.95	10.54	4.44	79.84	10.68	4.65
80.61	11.00	3.92	80.58	11.17	4.04
82.00	9.46	3.99	81.95	9.34	4.25
84.05	7.87	3.77	84.25	7.99	3.70
82.14	9.65	3.83	82.34	9.68	3.88

•••• from ethyl acetate.

the reaction mixture with ammonium chloride solution. The ethereal extract was dried with sodium sulfate and the substance was isolated after evaporation of the ether (variant A). When the substance was poorly soluble in ether, the latter was evaporated from the reaction mixture after its decomposition with ammonium chloride solution and the product (insoluble in the obtained aqueous solution) was filtered off and dried at room temperature (variant B). The substance was purified by crystallization from organic solvents. In the table are set forth the results of the action of some $R'MgX$ on benzoxazines.

2-(Benzylcyclohexylaminomethyl)-4-tert. butylphenol (VII) from N-benzylcyclohexylamine hydrochloride, formaldehyde and 4-tert. butylphenol. The starting N-benzylcyclohexylamine hydrochloride was prepared in the conditions described in [8] by reduction of N-cyclohexylidenebenzylamine with 99% HCOOH followed by treatment with hydrochloric acid. The hydrochloride was purified by crystallization from a mixture of isopropyl alcohol and ether and melted at 284-285° (block); the literature gives 252-253° [9] 284° [10].

For the preparation of (VII) successive addition of 2.25 g N-benzylcyclohexylamine hydrochloride, 0.4 g paraformaldehyde and 1.5 g 4-tert. butylphenol was made to a solution of 0.6 g KOH in 15 ml ethyl alcohol. The mixture was heated on a water bath, cooled and diluted with water. The separated product was crystallized from ethyl alcohol and then melted at 136.2-136.8°. A mixed test with the product of interaction of C_6H_5MgBr with (VI) did not give a melting point depression.

SUMMARY

1. Reaction of organomagnesium compounds with 3,4-dihydro-3-alkyl-6-alkyl(aryl)-1,3,2-benzoxazines results in opening of the benzoxazine ring with formation of the corresponding 2-(dialkylaminomethyl)-4-alkyl(aryl)-phenols as the main products.

2. The method in question may possess preparative interest, since it enables the introduction of a wider variety of substituents in the formed N-dialkylaminomethyl group.

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APPLICATION OF THE WILLGERODT REACTION TO THE SYNTHESIS OF SUBSTITUTED PHENYL- AND NAPHTHYLACETIC ACIDS

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Application of the Willgerodt reaction to the synthesis of a fairly large number of phenylacetic acids has been described in the literature [1]; in the majority of cases, however, the yields are not stated and it is therefore impossible to assess the value of this method for synthesis of a particular compound. More detailed data have been published on the preparation of thiomorpholides from substituted acetophenones [2,3,4,5], but due to the difficulty of saponification of the former, this modification of the Willgerodt reaction is little suited to the synthesis of the corresponding phenylacetic acids [6]. This reaction has not been applied, however, to the synthesis of substituted naphthylacetic acids. Moreover, the Willgerodt reaction is undoubtedly interesting for the synthesis in laboratory conditions of a whole series of substituted phenylacetic acids whose preparation is more complicated by other methods.

Nearly all of the phenyl- and naphthylacetic acids were prepared by us in standardized conditions: heating of ammonium polysulfide and the appropriate ketone in aqueous dioxane solution. Our experimental data on the preparation of phenyl- and naphthylacetic acids are set forth in Table 1.

It should be noted that it was not possible to obtain the corresponding amides and acids from o-hydroxyacetophenone, p-hydroxyacetophenone, 2,5-dibromoacetophenone, 2,4-dimethoxyacetophenone, 2,4,5-trichloroacetophenone, 4-bromonaphthyl-1-methyl ketone, 4-chloronaphthyl-1-methyl ketone, 4-methoxynaphthyl-1-methyl ketone and 4-ethoxynaphthyl-1-methyl ketone. The data of Table 1 permit of several generalizations about the effect of substituents in the aromatic radical on the course of the Willgerodt reaction. In spite of the abundant experimental material, this question has received very little attention in the literature. It has merely been reported that the presence of alkyl and alkoxyl and halogens has no appreciable influence on the course of the reaction [1], whereas nitro-, amino, formyl and similar groups may undergo changes due to the occurrence in the reaction medium of oxidation-reduction processes.

Our experimental data give definite indication of the influence of even such substituents as halogen and alkyl on the course of the Willgerodt reaction. The presence of one substituent in the phenyl radical in the para-position to the acetyl lowers the yield of the normal reaction products. The simplest substituents may be arranged in the following order of increasing unfavorable influence on the yield of products of the Willgerodt reaction:

$$CH_3 < Cl < CH_3O < I < OH$$

The main reaction product in the presence of such substituents as Cl, I and OCH_3 is a mixture of 2,4- and 2,5-substituted thiophenes.

Introduction of a second substituent into the aromatic radical suppresses the reaction of formation of thiophenes in consequence of which the yield of phenylacetic acids and their amides sharply increases. Thus, 4-methoxy-3-methyl- and 4-methoxy-2-methylacetophenones give considerably higher yields of normal products of reaction than 4-methoxyacetophenone, while nearly quantitative yields of amides and acids are got from some haloalkylacetophenones.

Accumulation of more than two halogens or other substituents in the aromatic radical of acetophenone leads to lowering of the yield of normal products of the Willgerodt reaction. In such a case the effect of halogens is particularly marked, the influence of methyl groups is considerably weaker.

A similar picture is observed in the naphthalene series. 4-Methyl-naphthyl-1-methyl ketone is converted in satisfactory yield into 4-methyl-naphthylacetamide, whereas the corresponding chloro-, bromo- and alkoxy ketones give mainly products of resinification. With ethyl-, propyl- and butyl-naphthylmethyl ketones the reaction proceeds normally but the yield of amides falls with increasing molecular weight of the hydrocarbon radical.

EXPERIMENTAL

Preparation of all of the amides of phenylacetic acids was performed in the following standard conditions: In a glass tube, volume about 100 ml, were placed 5 g ketone, 20 ml dioxane and 25 ml aqueous solution of ammonium polysulfide. The tube was placed in a stainless steel rotating autoclave and kept at 165-170° for 4 hours. After cooling, the reaction mixture was transferred to a porcelain beaker and evaporated on the water bath to dryness. The residue was twice extracted with hot water (each time with 200 ml). The precipitate of amide which came down on cooling the

aqueous extract was filtered off and recrystallized. The filtrate was evaporated to a small volume and a small additional amount of amide was thus obtained; in some cases, acidification of the mother liquor gave a small amount of acid which was filtered and recrystallized from water. In Table 2 are set forth the data for compounds not described in the literature.

TABLE 1

Prep. No.	Name of starting ketone	Yield (%) of amide	Yield (%) of acid	M.p. of amide	M.p. of acid
1	Acetophenone	88	5.5	–	–
2	4-Chloroacetophenone	28	7	175°[175]	105° [105.5]
3	4-Iodoacetophenone	12	0	•	135 [135]
4	4-Methylacetophenone	63	0	184 [185]	92 [92]
5	2-Hydroxyacetophenone	0	0	–	–
6	4-Hydroxyacetophenone	0	0	–	–
7	4-Methoxyacetophenone	25	0	175 [175]	85 [85]
8	2,5-Dibromoacetophenone	0	0	–	–
9	2,4-Dichloroacetophenone	39	5.5	•	•
10	2,5-Dichloroacetophenone	34.7	0	175 [175]	106 [106]
11	3-Methyl-4-bromoacetophenone	68	0	165 [168]	81 [81]
12	3-Methyl-6-bromoacetophenone	74.7	4	152 [152]	82 [82]
13	3-Methyl-4-chloroacetophenone	72.4	0	162 [162]	83 [83]
14	3-Methyl-6-chloroacetophenone	87.8	5.2	141 [141]	86 [85]
15	4-Methyl-2-chloroacetophenone	74.8	0	•	•
16	2-Methyl-4-methoxyacetophenone	59.2	0	•	107 [107]
17	3-Methyl-4-methoxyacetophenone	61.8	0	•	127 [127]
18	2,4-Dimethoxyacetophenone	0	0	–	–
19	2,4,5-Trichloroacetophenone	0	0	–	–
20	2,4,5-Trimethylacetophenone	42.1	0	165 [165]	118 [118]
21	Methyl-1-naphthyl ketone	87.8	0	182	132
22	4-Bromonaphthyl-1-methyl ketone	0	0	–	–
23	4-Chloronaphthyl-1-methyl ketone	0	0	–	–
24	4-Methylnaphthyl-1-methyl ketone	86.3	0	209 [209]	148 [148]
25	4-Methoxynaphthyl-1-methyl ketone	20	0	•	•
26	4-Ethylnaphthyl-1-methyl ketone	41	0	•	•
27	4-Ethoxynaphthyl-1-methyl ketone	0	0	–	–
28	4-Propylnaphthyl-1-methyl ketone	40	0	•	•
29	4-Butylnaphthyl-1-methyl ketone	34	0	•	•

Note: The melting points of amides and acids in brackets are literature data.

SUMMARY

1. Starting from the corresponding ketones, a study was made of the preparation of substituted phenyl and naphthylacetic acids by the Willgerodt reaction. A large number of compounds were used in the investigation.

2. It was established that the yield of arylacetic acids prepared by the Willgerodt reaction largely depends on the character of the substituents in the aromatic radical. In the simplest case, substituents unfavorably influencing the yield of arylacetic acids are arranged in the following order:

$$CH_3 < Cl < CH_3O < I < OH$$

Introduction of a second substituent into the aromatic radical leads to fall in the yield of normal products of the Willgerodt reaction.

3. A number of the synthesized compounds have not been described in the literature.

• See Table 2

TABLE 2

Prep.	Name of compound	Melting point		Analysis					
		acid	amide	Wt. of sample (g)	Amount of 0.02 N KOH or H_2SO_4 (ml) consumed	Molecular weight found	Molecular weight calculated	N content (%) found	N content (%) calculated
1	4-Iodophenylacetamide	–	191°	0.0624	11.81	–	–	5.30	5.36
2	2,4-Dichlorophenylacetic acid	131°	168	0.0652	16.15	201.9	204.8	–	–
			169	0.0532	13.24	201.0		–	–
3	2-Chloro-4-methylphenylacetic acid	106	164	0.0840	22.54	186.3	184.4	–	–
				0.0795	21.44	185.4		–	–
4	4-Methoxy-2-methylphenylacetamide	–	154	0.0742	20.19	–	–	7.62	7.80
				0.0720	19.64	–	–	7.64	
5	4-Methoxy-3-methylphenylacetamide	–	153	0.0690	19.00	–	–	7.71	7.80
				0.0698	18.67	–	–	7.49	
6	4-Methoxynaphthyl-1-acetic acid	144	175	0.1432	13.11*	218.5	216	–	–
				0.1238	11.28*	219.4		–	–
7	4-Ethylnaphthyl-1-acetic acid	129	167	0.0852	19.36	220.0	214	–	–
				0.0831	18.92	219.6		–	–
8	4-Propylnaphthyl-1-acetic acid	119	157	0.0892	19.30	231.0	228	–	–
				0.0901	19.35	232.8	–	–	–
9	4-Butylnaphthyl-1-acetic acid	110	156	0.0841	17.23	244.0	242	–	–
				0.0731	15.01	243.5		–	–

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SOME 9-SUBSTITUTED DERIVATIVES OF ACRIDINE

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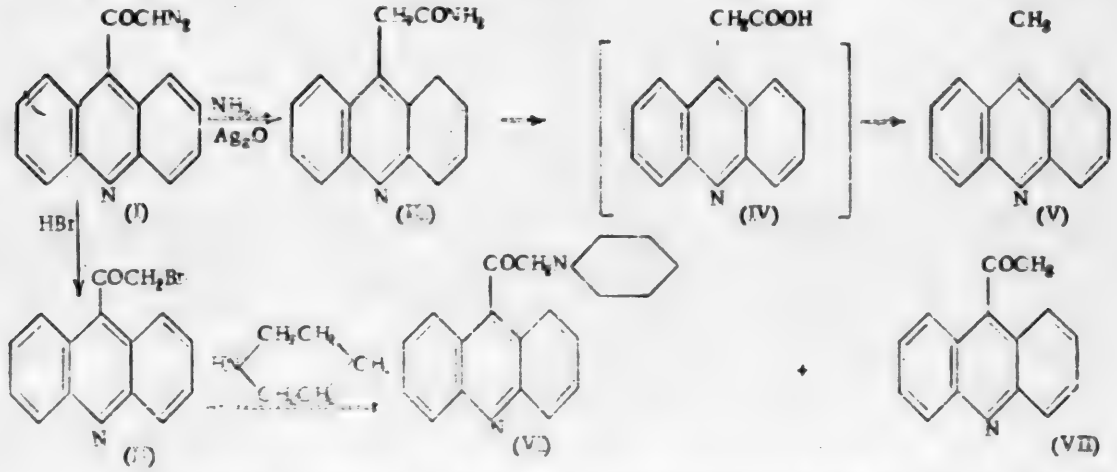
One of us in collaboration with T. V. Gortinskaya [1] has described 9-(diazoacetyl)-acridine (I), as well as acridyl-9-(ω-bromomethyl ketone) (II) which was prepared from diazoacetylacridine by the action of hydrogen bromide. Starting from these compounds, we undertook the synthesis of some previously unknown 9-substituted derivatives of acridine: from diazoacetylacridine we wished to obtained (by Wolff's method) acridyl-9-acetic acid (IV), while by condensation of acridyl bromomethyl ketone with secondary amines we aimed at obtaining the corresponding amino ketones.



Attempts to prepare acridylacetic acid directly from diazoacetylacridine were not crowned with success. It was therefore resolved first to prepare acridyl-9-acetamide (III) and then to saponify it to the acid. Transformation of diazoacetylacridine into acridylacetamide proceeds very smoothly and gives a yield of about 80% of the theoretical. On treating acridylacetamide with sodium nitrite in solution in a mixture of sulfuric and acetic acids, we actually succeeded in obtaining an acid whose analysis agreed fairly closely but not entirely satisfactorily, with that calculated for acridylacetic acid. With the aim of identifying this acid, it was converted into the hydrochloride of the acid chloride by the action of thionyl chloride in benzene solution; the acid chloride was then treated with concentrated aqueous ammonia to form the amide. The decomposition temperature of the latter proved to be 3° lower than that of the acridylacetamide prepared from diazoacetylacridine. A mixed sample of the two amides however gave a 20° depression of decomp. point. Attention was then directed to the fact that the conjectured acridylacetic acid, the hydrochloride of the acid chloride and the amide had decomposition temperatures respectively agreeing with those of acridine-9-carboxylic acid, the hydrochloride of its chloride, and the amide. It was further established that a mixture of the conjectured acridylacetic acid with authentic acridine-carboxylic acid, likewise a mixed sample of the amides of both acids, do not give a depression of the decomposition temperature, and that consequently the action of nitrous acid on acridylacetamide leads to acridine-carboxylic acid. The reason for this unexpected result became clear when acridylacetamide was subjected to hydrolysis in an alkaline or acid medium. Boiling of acridylacetamide with 20% hydrochloric acid gives a good yield of a substance which is insoluble in alkali and whose analysis, melting point and other properties indicate it to be 9-methylacridine (V). 9-Methylacridine is also formed by hydrolysis of acridylacetamide with alcoholic alkali, but side by side with acridone. Formation of 9-methylacridine in this case conclusively shows that hydrolysis of acridylacetamide does indeed give acridine-9-acetic acid, which is apparently unstable and undergoes decarboxylation to 9-methylacridine in the experimental conditions. If the reaction is performed with the help of a large excess of nitrous acid however, then the intermediately formed 9-methylacridine in the instant of its formation is oxidized to acridine carboxylic acid. In practice, brief heating of acridineacetamide with a small excess of nitrous acid gives 9-methylacridine.

Acridyl-9-(acetoxymethyl ketone), is obtained by reacting diazoacetylacridine with glacial acetic acid in presence of a small amount of copper acetate as catalyst. It is curious that this reaction does not take place in the absence of a catalyst.

The reaction of acridylbromomethyl ketone with piperidine proceeds in an unusual manner. On mixing a solution of acridylbromomethyl ketone in absolute benzene with an excess of piperidine at room temperature, piperidine hydrobromide soon starts to come down from the reaction solution, contaminated with a trace of acridone. After 6 hours the amount of piperidine hydrobromide is about 90% of the theoretical. On this basis we should expect that the condensation of the bromo ketone with piperidine is very complete. Actually, however, this is not the case. After separating the piperidine hydrobromide and driving off the benzene from the filtrate in vacuum, a syrup remains; trituration of the latter with methanol causes a compound with a decomposition temperature of about 130° to separate (precipitate A). It decomposes when recrystallization from methanol or absolute benzene is attempted and partly forms acridone. The same result is obtained when precipitate A is reprecipitated from chloroform by absolute ether at room temperature. Since the various attempts to purify precipitate A were unsuccessful, it was subjected to elementary analysis without purification. The results are close to those calculated for acridyl-9-(piperidinomethyl ketone) (VI). Moreover, it was possible to isolate (as chloroplatinate or picrate) another compound which unexpectedly proved to acridyl-9-(methyl ketone) (VII). After isolation in the free state from the picrate, this compound was identified by comparison with the acridylmethyl ketone prepared by oxidation of 9 α-(hydroxyethyl)-acridine with chromic acid mixture [2].

Debromination of acridylbromomethyl ketone by treatment with piperidine is, as far as we are aware, the first published case of debromination by an amine, of an α-bromo ketone containing the bromine at a primary carbon atom. A similar debromination by the action of piperidine on α-bromoketo esters containing bromine at a secondary or tertiary carbon atom was noted by Howk and McElvain [3] in the cases of α-bromo-α-benzoylacetoethyl, α-bromo-α-benzoylpropioethyl and α-bromo-α-benzoylphenylacetoethyl esters. In the first example, α,α-dipiperidinobenzoyl acetoethyl ester was formed together with the benzoylacetoethyl ester; in the second example, α, β-dipiperidinobenzoylpropioethyl ester was formed in addition to benzoylpropioethyl ester. The intermediate product in these reactions, in the opinion of Howk and McElvain is N-bromopiperidine; this would satisfactorily account for their results. The considerations of Howk and McElvain about intermediate formation of N-bromopiperidine appear to be corroborated by the isolation of nitromalonic ester and N-bromodimethylamine when bromonitromalonic ester is reacted with dimethylamine [4].

During the reaction of acridylbromomethyl ketone with piperidine, evidently N-bromopiperidine is likewise formed in part, and in the conditions of our experiment it reacts with excess of piperidine and gives piperidine hydrobromide. Although little study has been made of the properties of N-bromopiperidine, we nevertheless know that it behaves like N-chloropiperidine, the latter is known to decompose on standing with release of the hydrogen halide of piperidine, while with alcoholic KOH it gives KCl and tripiperideine[5]. Consequently we can understand why the yield of piperidine hydrobromide in our case reaches 90% of the theoretical, whereas the yield of the amino ketone (precipitate A) is only about 25% on the average.

In order to verify whether piperidine exercises a specific action on acridylbromomethyl ketone, a similar experiment was run with diethylamine in place of piperidine. In this case also, we obtained acridylmethyl ketone, diethylamine hydrobromide (65% of the theoretical) and a considerable amount of acridone. Acridine 9-(diethylaminomethyl ketone) could not be isolated. This is probably because the reaction solution was allowed to stand for too long a period, in consequence of which the formed amino ketone was able to decompose and form acridone.

Debromination of α bromo ketones by piperidine in the above indicated cases should undoubtedly be correlated with the known ability of α-bromo ketones to undergo debromination according to the reversible reaction:

$$RCOCHBrR' + HBr \rightleftarrows RCOCH_2R' + Br_2,$$

in which the equilibrium is more or less shifted to the right or to the left, depending on the structure of the bromo ketone. In the presence of a bromine acceptor (phenol, β naphthol or cyclohexene), debromination is very complete [6]. Thus, even ω-bromoacetophenone, which is unaffected by hot concentrated hydrobromic acid, is almost completely transformed into acetophenone in a medium of a 33% HBr solution in glacial acetic acid in presence of β naphthol; the equivalent amount of α-bromo-β-naphthol is formed [6a].

On the basis of the foregoing remarks, the idea suggests itself that debromination of α bromo ketones by amines cannot be such a rare phenomenon as appears to be the case from the small number of examples reported up to now.

All of the decomposition temperatures reported in this paper were determined as a rule by first heating the capillary rapidly and then, from 40-50°, maintaining a temperature rise of 4° per minute.

EXPERIMENTAL

Acridyl-9-acetamide

Into a three-necked, 100 ml flask fitted with stirrer, mercury seal and reflux condenser are charged 65 ml alcohol, 18 ml conc. aqueous ammonia and 3 ml 10% silver nitrate solution. The mixture is heated to 70-75°, and at this temperature, with stirring, is added (in small portions over a period of 2 hours) 3 g finely pulverized 9- (diazoacetyl)-acridine, the course of the reaction being checked by the evolution of nitrogen. After the reaction solution has completely cooled, the lustrous, dark-brown, fine needles are filtered off and washed with dilute ammonia solution and then with water. Yield of acridylacetamide 2.3 g or 80% of the theoretical. Decomposition point 258-260°.

For analysis, the acridylacetamide was recrystallized from a small quantity of alcohol. White (with a greenish tinge), coalescent needles with decomposition point 260-261°. Acridylacetamide is soluble in glacial acetic acid and in mineral acids; it is reprecipitated unchanged by adding alkali to its solutions in acids prepared in the cold or with gentle heating; purification may be effected by this procedure.

2.895 mg substance: 8.070 mg CO_2, 1.275 mg H_2O. 2.360 mg substance: 0.250 ml N_2 (24°, 743 mm). Found %: C 76.02; H 4.93; N 11.90. $C_{15}H_{12}ON_2$. Calculated %: C 76.24; H 5.12, N 11.86.

9-Methylacridine from Acridyl-9-acetamide

a) By the action of hydrochloric acid. 1 g acridylacetamide is dissolved in 30 ml 20% hydrochloric acid and refluxed for 1½ hours. The yellow solution is filtered and 12% aqueous ammonia is added until alkaline. The precipitate weighs 0.8 g. M.p. 115-117°. Recrystallization from aqueous alcohol gives lustrous light-yellow needles which lose their luster when dried in the vacuum-desiccator; m.p. 118-119°. A mixed test with a sample of 9-methylacridine does not give a depression.

Found %: C 86.89; H 5.52; N 7.51. $C_{14}H_{11}N$. Calculated %: C 87.01; H 5.74; N 7.25.

b) By the action of alcoholic alkali. 1 g acridylacetamide is boiled for 10 hours with 25 ml 25% solution of KOH in methyl alcohol. At the end of the heating, the whole of the amide goes into solution with a dark, yellowish-green color. The solution is evaporated to dryness in vacuum and the residue is heated with water, drained at the pump and well washed. The dried residue is dissolved in boiling ethyl alcohol; green needles of acridone separate from the filtrate; its m.p. and its mixed m.p. are both 353-354°. After separation of the acridone, the alcoholic mother liquor is diluted with water and yields 0.22 g 9-methylacridine with m.p. 116-117°.

c) By action of nitrous acid. 1 g acridylacetamide is dissolved in 12 ml 96% acetic acid and the solution filtered if necessary; addition is made of 1.8 ml 91% sulfuric acid and the mass is heated to 70°. At this temperature and with stirring, dropwise addition is made of 2 ml 20% sodium nitrite solution, heating is continued for a further 5 minutes and the mass is poured into 50 ml water. The homogeneous solution is made slightly alkaline with dilute KOH solution. The light-yellow precipitate of 9-methylacridine melts at 115-116° after recrystallization from aqueous alcohol.

Acridyl-9-carboxylic Acid from Acridyl-9-acetamide

0.85 g acridylacetamide is dissolved in 12 ml 96% acetic acid, 1.8 ml 91% sulfuric acid is added, following gradually, at room temperature and with stirring, by 2.4 g finely pulverized sodium nitrite. The temperature of the solution is then slowly raised to 75-80° and held there for 2 hours. After cooling, the reaction mixture is run into 100 ml cold water; the amorphous yellow precipitate of the acid is drained at the pump and twice purified through its sodium salt. For this purpose the acid is dissolved in NaOH, filtered, and acidified with dilute hydrochloric acid until the reaction is acid to Congo. The obtained acid weighs 0.15 g and has decomposition point 279-281°. After recrystallization from glacial acetic acid the decomposition point is 283-284°. This is also the decomposition point of its mixture with an authentic specimen of acridine-9-carboxylic acid.

Found %: C 74.68; H 4.39. $C_{14}H_9O_2N$. Calculated %: C 75.31, H 4.07.

0.2 g acid prepared by the above described method and purified through the sodium salt is boiled with a mixture of 1 ml thionyl chloride and 1.2 ml absolute benzene until a homogeneous solution is formed. The excess of thionyl chloride and benzene are distilled off, fresh benzene is added to the residue and again distilled off; this operation is repeated 2-3 times. The dry residue is well washed with benzene and dried. Yield of the hydrochloride of acridine-9-carboxylic acid chloride 0.1 g. Decomposition point 214-215°.

0.15 g of the carboxylic acid chloride hydrochloride is mixed with 10 ml conc. aqueous ammonia, gently heated on the water bath and left overnight. The precipitate, which is no longer crystalline, is drained, washed with water and recrystallized from alcohol. Decomposition point 263-264°. A mixed test with the amide of acridine-9 carboxylic acid prepared by hydrolysis of 9-cyanoacridine [7] does not give a depression. A mixed sample with acridyl-9-acetamide melts at 240-242° with decomposition.

Acridyl-9-(acetoxymethyl Ketone)

6 ml glacial acetic acid to which has been added a few crystals of copper acetate, is heated to the boil under a reflux condenser, and to the boiling solution is added 1 g 9-(diazoacetyl)-acridine dropwise over a period of 30 minutes. Vigorous evolution of nitrogen soon commences and about 75 ml is collected. After completion of the addition of the diazoacetylacridine, the dark-brown solution is boiled for another few minutes. The cooled solution is heavily diluted with ether and the crystalline precipitate of acridyl-9-(acetoxymethyl ketone) is filtered at the pump. Weight 0.45 g, m.p. 178-179°. A further 0.2 g can be isolated from the mother liquor after evaporation. Same m.p.

After recrystallization from alcohol the pure substance melts at 183-184°. Acridyl-9-(acetoxymethyl ketone) is slightly soluble in benzene and chloroform, almost insoluble in ether and ligroine, soluble in inorganic acids.

3.655 mg substance: 9.808 mg CO_2; 1.554 mg H_2O. Found %: C 73.18; H 4.76. $C_{17}H_{15}O_3N$. Calculated %: C 73.09, H 4.69.

Reaction of Acridyl-9-(ω-bromomethyl ketone) with Piperidine

3 g acridyl-bromomethyl ketone with m.p. 148-150° is dissolved with heating in 53 ml benzene (previously dried over sodium); to the cooled solution is added 3.9 ml dry piperidine and the mass is left in a dark place at room temperature for 6 hours. The crystalline precipitate is filtered, washed with dry benzene and dried. Weight 1.6 g. Treatment with cold water brings the greater part of the material into solution; after driving off the water from the filtrate and recrystallizing from chloroform, the product melts at 234-235°, which is the m.p. of piperidine hydrobromide. The water-insoluble portion, weight about 0.1 g, melts (after purification by sublimation) at 353° and does not give a depression in admixture with acridone.

Evaporation of the benzene filtrate of the reaction solution in vacuum at a temperature not exceeding 30-35° leaves a dark syrup smelling of mice. Trituration of the residue with 20 ml methanol causes separation of 0.65-0.85 g greenish-yellow precipitate (A); this is filtered at the pump and washed several times with methanol. This precipitate melts at 127-130° with decomposition to a dark liquid which rises in the capillary at about 136°. Sparingly soluble in ether, ligroine, benzene and methyl and ethyl alcohols, soluble in the cold in chloroform and glacial acetic acid. An attempt to purify it by recrystallization from benzene or methyl alcohol led to separation from the solution of a small quantity of acridone, removal of the solvent from the filtrate in vacuum at 30-35° gave a dark brown oily residue. In most cases a similar result is obtained by reprecipitation with dry ether of the cold prepared solution of precipitate A in a small quantity of dry chloroform. The elementary analysis of the unpurified precipitate A gives results in fairly close agreement with those calculated for acridyl-9-(piperidinomethyl) ketone.

2.952 mg substance: 8.151 mg CO_2; 1.612 mg H_2O. 3.212 mg substance: 9.615 mg CO_2; 1.830 mg H_2O. 2.385 mg substance: 0.256 ml N_2 (21°, 739.0 mm). 4.085 mg substance: 0.324 ml N_2 (22°, 732.8 mm). Found %: C 80.19, 78.36; H 6.61, 6.38; N 8.87, 8.80. $C_{19}H_{20}ON_2$. Calculated %: C 78.90, H 6.62, N 9.21.

The combined transparent methanol solutions obtained after separation and washing of precipitate A with a total volume of 30-40 ml are acidified with 4 ml 10% alcoholic solution of HCl and precipitated with 40 g of 10% alcoholic solution of platinum chloride. After addition of one-third of the platinum chloride the solution is decanted from the resinous precipitate; this operation is repeated once, and then the remaining platinum chloride is added; after a few hours the chloroplatinate is filtered off and twice recrystallized from 3% hydrochloric acid; decomposes with [illegible] with preliminary darkening.

4.005 mg substance: 7.665 mg CO_2; 1.115 mg H_2O. 4.035 mg substance: 0.157 ml N_2 (22°, 751 mm). 1.615 mg substance: 4.322 mg AgCl. 10.915 mg substance: 2.400 mg residue after ignition; 0.1200 g substance on loss of weight: 4.8 mg (100°, P_2O_5). Found %: C 40.88; H 3.12, N 1.45, Cl 23.16, Pt 21.99, volatiles 4.0.

The analytical data, with the exception of the nitrogen content, are in agreement with those calculated for the chloroplatinate of acridyl-9-(methyl ketone) crystallizing with two molecules of water: $C_{16}H_{14}O_3N.Cl.Pt$. Calculated %: C 40.53, H 3.18, N 3.15, Cl 23.95, Pt 21.98, volatiles 4.05.

The following results for the elementary analysis were obtained after drying in a tube-type desiccator over P_2O_5 at 100°:

3.628 mg substance: 8.618 mg CO_2; 0.995 mg H_2O. 4.090 mg substance: 4.192 mg AgCl. 14.130 mg substance: 3.205 mg residue after ignition. Found %: C 42.17; H 3.07; Cl 25.35; Pt 22.67. $C_{28}H_{24}O_2N_2Cl_4Pt$. Calculated %: C 42.24; H 2.84; Cl 24.97; Pt 22.91.

On adding an alcoholic solution of picric acid to the methanol solution prepared after separation of precipitate A and acidified with 2.1 ml alcoholic HBr solution, the picrate of acridyl-9-(methylketone) comes down; this recrystallizes from methanol in the form of dark-brown (nearly black) needles with decomposition point 245-246°.

2.604 mg substance: 5.347 mg CO_2; 0.768 mg H_2O. 3.335 mg substance: 0.372 ml N_2 (28°, 732.5 mm). Found %: C 56.0; H 3.30; N 12.19. $C_{22}H_{16}O_8N_6$. Calculated %: C 55.99; H 3.13; N 12.45.

The free base obtained from the picrate with the help of hydrochloric acid has m.p. 101-103° (light-yellow needles) after recrystallization from ligroine (b.p. 50-75°).

Found %: C 81.78; H 4.90; N 6.74. $C_{15}H_{11}ON$. Calculated %: C 81.42; H 5.0; N 6.34.

Acridyl-9-(methyl ketone), prepared by Eisleb's method [2] by oxidation of 9-(α-hydroxyethyl)-acridine with chromic acid mixture, also melts at 101-103° and not at 109° (as reported by Eisleb) and does not give a depression in the mixed melting determination.

Reaction of Acridyl-(9-ω-bromomethyl Ketone) with Diethylamine. 6 g acridylbromomethyl ketone is mixed with a solution of 9 ml diethylamine in 105 ml dry benzene. After an hour's boiling the initially pink solution is colored dark-red. After keeping for 40 days at room temperature, 4.5 g yellowish green precipitate was obtained, consisting of a mixture of diethylamine hydrobromide and acridone (1.7 g). The benzene filtrate was evaporated to dryness in vacuum at 30-35°; the residue was dissolved in 20 ml cold methyl alcohol and filtered from the small amount of insoluble material, and 2.1 ml of 31% HBr solution in absolute alcohol was added to the filtrate. On standing, this solution deposited a small quantity of a substance which crystallized indefinitely and had decomposition point 192-195°. It was not further investigated. The filtrate from this solid was fractionally precipitated with an alcoholic solution of picric acid. After removal of the initially separated resinous impurities, the picrate was recrystallized from methanol. Long, star-shaped clusters of dark needles with decomposition point 245-246°. A mixed test with the picrate of acridyl-9-(methyl ketone) does not give a depression.

Found %: C 56.63; H 3.40; N 12.32. $C_{22}H_{16}O_8N_6$. Calculated %: C 55.99; H 3.13; N 12.45.

SUMMARY

1. Treatment of 9-(diazoacetyl)-acridine with ammoniacal silver nitrate solution gives acridyl-9-acetamide. Hydrolysis of the latter with hydrochloric acid or alcoholic alkali gives 9-methylacridine as a result of decarboxylation of the intermediately formed acridyl-9-acetic acid. The action of a large excess of sodium nitrite on acridylacetamide in a mixture of sulfuric and acetic acids gives acridone-9-carboxylic acid.

2. Reaction of 9-(diazoacetyl)-acridine with glacial acetic acid in presence of copper acetate as catalyst gives acridyl-9-(acetoxymethyl ketone). This reaction could not be effected in the absence of a catalyst.

3. Reaction of acridyl-9-(ω-bromomethyl ketone) with piperidine gave a compound which could not be purified and whose analytical data were close to those calculated for acridyl-9-(piperidinomethyl ketone). Acridone and acridyl-9-(methyl ketone) were isolated in addition. Similarly the reaction of acridyl-9-(ω-bromomethyl ketone) with diethylamine gave acridone and acridyl-9-(methyl ketone).

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COPLANARITY OF THE NITRO GROUP WITH THE BENZENE RING AND ITS INFLUENCE ON THE COLOR OF DYES

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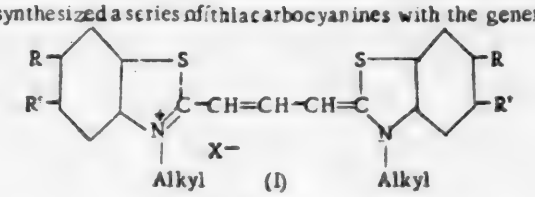
The influence of the nitro group on the color of organic dyes is bound up with its ability to repel electrons from the benzene ring and also from the conjugation chain of the dye. On displacement of the electrons from the benzene ring to the oxygen atoms of the nitro group, the bond between the nitrogen atom of the nitro group and the benzene ring acquires the character of a double bond. A necessary condition for such a displacement of electrons is the arrangement of the nitro group in the same plane as the benzene ring.* If a voluminous substituent is introduced in the ortho position to the nitro group, its effect on light absorption must be reduced or entirely disappear, as actually occurs in ortho-substituted aromatic nitro compounds which absorb in the ultraviolet [2]. The influence of ortho-substituents on the auxochromic activity of the nitro group in the visible region has not been investigated. We undertook a study of this influence with reference to cyanine dyes and azo dyes.

For this purpose we synthesized a series of thiacarbocyanines with the general formula (I):



whose absorption maxima and molecular extinctions are set forth in Table 1 (dyes 1, 2, 4, 5 are listed for comparison).

TABLE 1

No. of dye	R	R'	Alkyl	$\lambda_{max.}$ in mμ	$\epsilon \cdot 10^{-4}$
1	H	H	C_2H_5	558	16.5
2	H	CH_3	C_2H_5	565	14.0
3	H	C_2H_5	CH_3	565	15.0
4	H	$C(CH_3)_3$	CH_3	565	14.4
5	NO_2	H	C_2H_5	584	13.7
6	NO_2	CH_3	C_2H_5	582	16.8
7	NO_2	C_2H_5	CH_3	580	16.9
8	NO_2	$C(CH_3)_3$	C_2H_5	570	16.3

The absorption curves of dyes 1, 4, 5, 6, 7, and 8 are plotted in Figure 1.

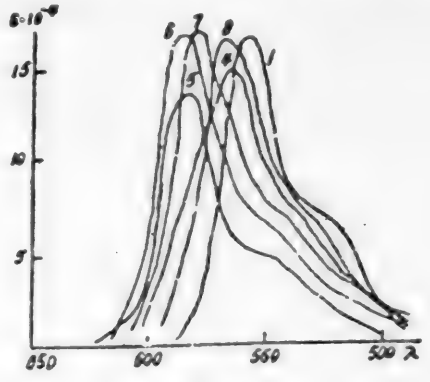
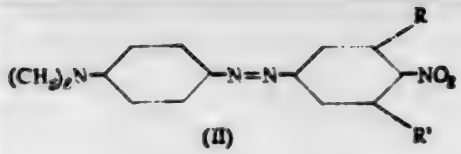


Figure 1

Introduction of a methyl group in the ortho-position to the nitro group (6) hardly changes the absorption curve. The ethyl group also has little effect on the color of the nitro dye (7). But the voluminous tertiary butyl group almost completely eliminates the auxochromic activity of the nitro group: the absorption maximum of dye 8 is shifted into the long-wave region by 5 mμ in comparison with dye 4 which does not contain a nitro group.

The same is observed with azo dyes. We synthesized three dyes with the general formula (II) and determined their absorption maxima and molecular extinctions (Table 2). The absorption curves of these compounds are plotted in Fig. 2.

* This problem is considered in more detail in a paper by one of us on the coplanarity of the dimethylamino group with the benzene ring [1].



(II)

We see from Table 2 and Fig 2 that one methyl group in the ortho position to the nitro group has little effect on the absorption maximum and the shape of the absorption curve (10). The introduction of a methyl group in the second ortho-position, however, causes the maximum to shift by 32 mμ in the short-wave direction (11).

It is interesting that in both the cyanine and the azo dyes the introduction of substituents in the orthoposition to the nitro group mainly affects the absorption maximum of the dye and has little effect on the intensity of absorption.

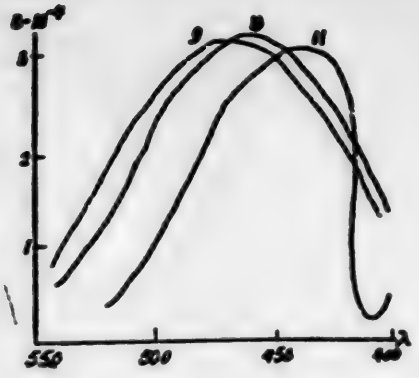


Figure 2

TABLE 2

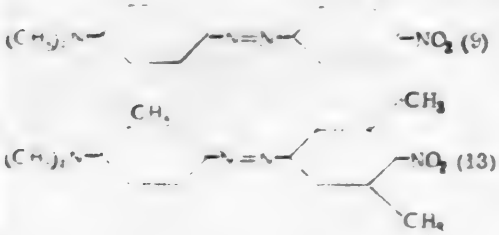
No of dye	R	R'	$\lambda_{max.}$ (in mμ)	$\epsilon \cdot 10^{-4}$
9	H	H	475	3.2
10	H	CH_3	460	3.2
11	CH_3	CH_3	443	3.1

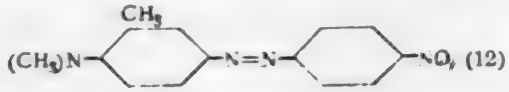
TABLE 3

No. of dye	$\lambda_{max.}$ (in mμ)	$\epsilon \cdot 10^{-4}$
9	475	3.2
12	438	2.2
13	418	3.5

In previous communications [3, 4] we showed that the methyl group has a strong influence on the auxochromic activity of the dimethylamino group. On the nitro group the methyl group has either no effect at all or a very weak one. An appreciable effect is manifested only by the tertiary butyl group or by two methyl groups. This was to be expected because the nitro group occupies a smaller volume than the dimethylamino group,* and is therefore exposed to a lesser degree to the action of the adjacent substituents.

In Table 3 are set forth the absorption maxima and molecular extinctions of dyes 9, 12 and 13





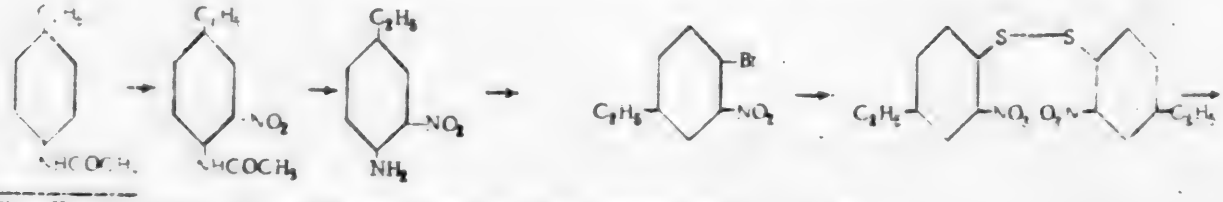
As was also to be expected, the least displacement of the maximum is observed in the case of dye 13 in which both of the auxochromes – the dimethylamino and the nitro group – are moved out of the plane of the molecule

The synthesis of the bases required for the preparation of dyes with the general formula (I) – 2,5-dimethyl-6-nitrobenzothiazole (III) and 2-methyl-5-tert.butyl-6-nitrobenzothiazole (IV) –

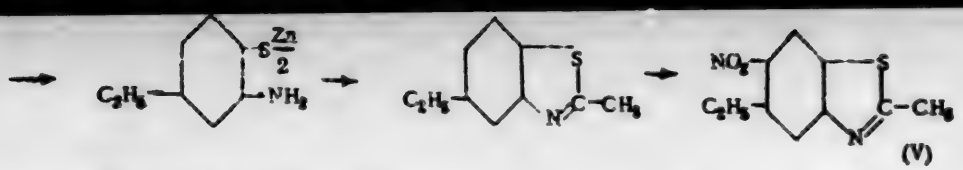
(III)

(IV)

has been described previously [3]. 2-Methyl-5-ethyl-6-nitrobenzothiazole (V) was prepared by the following route



* The effective radius of the methyl group is 2A, that of the oxygen atom is 1.4 A [5].



(V)

Nitration of 2-methyl-6-ethylbenzothiazole gives two nitro products: one with m.p. 100-102° and the second with m.p. 94-96°. The quaternary salt prepared from the nitro product with m.p. 100-102° gives with ethyl orthoformate a nitrothiacarbocyanine with an absorption maximum of 580 mμ, reduction of which with tin chloride gives an aminothiacarbocyanine with an absorption maximum of 590 mμ. On the basis of the considerations expounded in one of the previous papers [3] we assign structure (V) to the compound with m.p. 100-102°. The nitro product with m.p. 94-96° is probably 2-methyl-4-nitro-5-ethylbenzothiazole.

From the quaternary salts of bases (III to V) were prepared dyes 6, 7 and 8; from the quaternary salt of 2-methyl-5-ethylbenzothiazole was prepared dye 3.

EXPERIMENTAL

Intermediate Products

2-Methyl-5-ethylbenzothiazole. 33 g 3-nitro-4-bromoethylbenzene [6] was dissolved in 70 ml alcohol; addition was made of a hot mixture of 19 g crystalline sodium sulfite 2.8 g sulfur and 20 ml alcohol. The mixture was boiled for 2 hours. 2,2'-Dinitro-4,4'-diethyldiphenyldisulfide came down in the form of an oil which later crystallized. Yield 21.5 g. 21.5 g disulfide was mixed with 120 ml glacial acetic acid. Gradual addition was made, with energetic stirring, of 42 g zinc dust and 90 ml conc. HCl. Stirring was continued for another hour; the solution was filtered, diluted with water and saturated with sodium acetate. The white precipitate of zinc mercaptide was filtered and dried. The 17.5 g of mercaptide was heated for 2 hours with an excess of acetic anhydride. Water was added to the solution; the mixture was gently heated for decomposition of the excess of acetic anhydride and made alkaline. The 2-methyl-5-ethylbenzothiazole separated in the form of an oil and was extracted with benzene and distilled in vacuum. Yield 10 g or 59%, calculated on the mercaptide.

Picrate: yellow needles (from alcohol), m.p. 165-167°.*

Found %: N 13.35, 13.51. $C_{16}H_{14}O_7N_4S$. Calculated %: N 13.79.

Methiodide: colorless tablets (from alcohol), m.p. 199-201°.

Found %: I 39.95, 40.01. $C_{11}H_{14}NSI$. Calculated %: I 39.81.

2-Methyl-5-ethyl-6-nitrobenzothiazole (V). 6 g 2-methyl-5-ethylbenzothiazole was added dropwise with stirring to a mixture of 4.8 ml HNO_3 (s.g. 1.4) and 12 ml concentrated H_2SO_4. The mixture was then stirred for 20 minutes on the water bath and poured onto ice. The solidified nitroproduct was filtered, dissolved by heating in concentrated HCl and filtered from insoluble resinous impurities. The crystalline nitro product came down when the filtrate was diluted with water. Yield of crude product 4 g, m.p. 70-72°. Repeated crystallization from alcohol gave 0.9 g nitro product with m.p. 100-102°. The nitro product isolated from the alcoholic mother liquor was dissolved in concentrated HCl, the solution was diluted with double the amount of water and the precipitate was filtered. The product remaining in solution was separated by heavy dilution with water. By numerous repetitions of this procedure it was possible to resolve the product from the mother liquor into two fractions: with m.p. 100-102° (0.6 g) and with m.p. 94-96° (0.6 g). In this manner 1.5 g nitro product with m.p. 100-102° and 0.6 g with m.p. 94-96° were isolated. A mixture of both preparations melts at 74-76°. To the nitro product with m.p. 100-102° we assigned the structure of 2-methyl-6-ethyl-6-nitrobenzothiazole, to the nitro product with m.p. 94-96° the structure of 2-methyl-4-nitro-5-ethylbenzothiazole.

The 6-nitro isomer. Found %: N 12.83, 12.78. $C_{10}H_{10}O_2N_2S$. Calculated %: N 12.61.

Dyes

Bis-[3-methyl-5-ethylbenzothiazole (3)]-trimethine-cyanine methiodide (3). 0.3 g 2-methyl-5-ethylbenzothiazole methiodide, 0.3 g ethyl orthoformate and 3 ml pyridine were boiled for 30 minutes. The precipitated dye (greenish needles) was filtered, washed with hot alcohol and dried. M.p. 260-262°. Yield 0.12 g or 50% of the theoretical.

Found %: I 24.07, 24.14. $C_{25}H_{29}N_2S_2I$. Calculated %: I 24.44.

* All the melting and boiling points in this paper have been corrected.

Bis [3-ethyl-5-methyl-6-nitrobenzothiazole (2)]-trimethinecyanine-p-toluenesulforate (6). 0.2 g 2,5-dimethyl-6-nitrobenzothiazole and 0.2 g ethyl p-toluenesulfonate were heated for 4 hours at 160-170°. The solidifying dark mass was dissolved in water and boiled several times with carbon until perfectly colorless. The solution was evaporated to dryness. Yield of salt 0.15 g or 42.5% of the theoretical.

0.1 g of the quaternary salt was boiled for 20 minutes with 0.1 g ethyl orthoformate in pyridine. The dye was precipitated by ether, filtered and recrystallized from alcohol. Green tablets with a metallic luster, m.p. 267-268° with decomposition. Yield 0.035 g or 47% of the theoretical.

Found %. N 8.40, 8.60. $C_{30}H_{30}O_4N_4S_3$. Calculated %: N 8.56.

Bis-[3-methyl-5-ethyl-6-nitrobenzothiazole (2)]-trimethinecyanine methosulfate (7). 0.2 g 2-methyl-5-ethyl-6-nitrobenzothiazole and 0.12 g dimethylsulfate were heated for 2 hours at 100°. The resultant methosulfate was boiled for 30 minutes in pyridine with 0.3 g ethyl orthoformate. The precipitated dye was filtered, washed with hot alcohol and dried. Yield 0.12 g (30%). Violet needles, m.p. above 300°.

Found %: N 9.26, 9.30. $C_{34}H_{34}N_4S_3$. Calculated %. N 9.43.

Bis-[3-ethyl-5-tert butyl-6-nitrobenzothiazole (2)]-trimethinecyanine-p-toluene-sulfonate (8). 0.2 g 2-methyl-5-tert. butyl-6-nitrobenzothiazole and 0.2 g ethyl p-toluenesulfonate were heated for an hour to 150-160°. The formed crystals were washed with benzene and dried. Yield of quaternary salt 0.3 g or 75% of the theoretical. 0.2 g salt was boiled in pyridine with 0.2 g ethyl orthoformate for 20 minutes. The dye was precipiated with ether, filtered and recrystallized from alcohol. Green needles, m.p. 277° with decomposition. Yield 0.11 g or 69% of the theoretical.

Found % N 7.45, 7.30. $C_{36}H_{42}O_2N_4S_3$. Calculated % N 7.59.

4-Dimethylamino-3'-methyl-4'-nitroazobenzene. 0.4 g 3-methyl-4-nitroaniline [7] was diazotized and added to a cooled solution of 0.4 g dimethylaniline in dilute hydrochloric acid. After a few hours, the dye was filtered, dissolved with heating in strong HCl, filtered from insoluble impurities and precipitated with ammonia. Yield of crude dye 0.3 g (40%). Purification was effected by chromatography of benzene solution on alumina. After chromatography the dye was obtained in the crystalline state with m.p. 160°. It was recrystallized from benzene as brown needles m.p. 160-162

Found % N 19.84, 19.98 $C_{15}H_{16}O_2N_4$. Calculated %. N 19.72.

4-Dimethylamino-3',5'-dimethyl-4'-nitroazobenzene (11). 0.3 g 3,5-dimethyl-4-nitroaniline [8] was diazotized and added to a cooled solution of 0.3 g dimethylaniline in dilute HCl. After a few minutes addition was made of 2 g sodium acetate. The precipitated dye was filtered and crystallized from alcohol. Red needles, m.p. 176-178°. Yield 0.3 g or 50% of the theoretical

Found % N 18.89, 18.82 $C_{16}H_{18}O_2N_4$. Calculated %. N 18.79.

3,3',5'-Trimethyl-4-dimethylamino-4'-nitrozobenzene (13). 0.3 g 3,5-dimethyl-4-nitroaniline was diazotized and added to a cooled mixture of 0.3 g dimethyl-o-toluidine, 5 ml alcohol and 2 g crystalline sodium acetate. The dye was filtered and crystallized from alcohol. Yield 0.25 g (46%). Orange needles, m.p. 112-114°.

Found % N 18.02, 18.24 $C_{17}H_{20}O_2N_4$. Calculated % N 17.95.

SUMMARY

1. A study was made of the effect of steric hindrance on the auxochromic activity of the nitrogroup in cyanine dyes and azo dyes containing nitro groups.

2. It was established that methyl and ethyl groups in the ortho-position to the nitro group weakly influence the absorption. The more voluminous tertiary butyl group almost completely suppresses the auxochromic activity of the nitro group. Two methyl groups in the ortho position to the nitro group have an influence similar to that of the tertiary butyl group

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INVESTIGATION OF THE ALKALOIDS OF LEONTICE EWERSMANNII BGE

I. A NEW ALKALOID TASPINE AND THE ALKALOID ISOLEONTINE. PREPARATION OF LEONTIDANE AND ISOLEONTANE

T. F. Platonova, A. D. Kuzovkov and P. S. Massagetov

"Leontik" or Lion's tail (Leontice Ewersmannii Bge) belongs to the family of the Berberidacea indigenous to Soviet Central Asia, Iran and Afghanistan. The presence of alkaloids in the plant was first established by P. S. Massagetov in 1926 [1]. The study of the alkaloids was commenced by A. P. Orekhov and R. A. Konovalova [2]. In 1932 they reported the isolation from the plant of three alkaloids: leontamine, leontidine, and a third substance in the form of its picrate with m.p. 178-180°. Of these three alkaloids, only the composition of leontamine was established, and the formula $C_{14}H_{24}N_2$ was assigned to it. The investigation was continued by S. Yu. Yunusov and L. G. Sorokina [3] who obtained a new alkaloid, leontine, with the composition $C_{18}H_{34}ON_2$; for leontidine they proposed the formula $C_{15}H_{30}ON_2$ and they obtained more accurate values for the constants of the base and its salts. The authors also isolated the alkaloids pachycarpine and lupanine from the plant.

The availability of the wild-growing lion's tail and its high content of organic bases prompted us to return to the study of the alkaloids of this plant. From the above-ground parts, gathered during the flowering period and containing a total of 0.77% alkaloids, we isolated leontidine (0.13%), pachycarpine (0.02%) and L-lupanine (0.003%). These alkaloids had previously been found in the plant. Fractional distillation in vacuum gave a base whose boiling and melting points were close to those of leontine and with the same composition. The melting point of the methiodide and perchlorate also appeared to confirm the identity between our isolated base and leontine. This assumption had to be rejected however after our base was found to be optically active. Having been unable so far to establish whether this substance is an optically active form of leontine or a new alkaloid, we propose for it the name of isoleontine. The constants of leontine and isoleontine are compared in Table 1.

TABLE 1

	Base			Perchlorate	Methiodide	Picrate
	m.p.	b.p.*	$[\alpha]_D$	m.p.	m.p.	m.p.
Leontine $C_{18}H_{34}ON_2$	103-104°	195-205° (7 mm)	0°	232°	290-292°	—
Isoleontine $C_{18}H_{34}ON_2$	107-108	175-200 (3 mm)	−78.2	252	297	177-179°

* Boiling point of the fraction from which the base was isolated.

The specimen of the plant that we investigated contained 1.03% isoleontine. It should be noted that the melting point of isoleontine picrate agrees with that of the picrate prepared by Orekhov and Konovalova in the first investigation of the plant. Isoleontine was evidently also obtained for the first time by the cited authors in the form of its picrate.

In addition to the four bases mentioned above we also isolated an alkaloid which differed markedly from the other alkaloids of this plant by virtue of the insolubility in water of the sulfate, hydrochloride and other salts with inorganic acids. The base* melts (with decomp.) 370°; the substance is insoluble in water and solutions of caustic alkalies, soluble in chloroform and dichloroethane; it is optically inactive. The composition of the base corresponds to the formula $C_{19}H_{29}O_3N$. The sulfate has the composition $C_{19}H_{29}O_3N \cdot 0.5H_2SO_4 \cdot H_2O$; it crystallizes from a large quantity of hot water (1:400) in the form of thin white needles melting at 360°. The alkaloid contains two methoxyl, one methylenedioxy and two methyl groups linked to nitrogen. It forms a crystalline methiodide $C_{19}H_{29}O_3N \cdot CH_3I \cdot H_2O$. The nitrogen atom is evidently tertiary and in an open chain. All of the stated properties show that the alkaloid is a new one, and we therefore propose for it the name of taspine (from the Uzbek name "taspi" for lion's tail). Alkaline hydrolysis of taspine gave an amino acid with the composition $C_{19}H_{31}O_4N \cdot H_2O$. Its formation not involving

* Crystallized from toluene; form—light yellow needles.

a change in the number of carbon atoms in the molecule, points to the presence of a lactone group, and this is confirmed by transformation of the amino acid into taspine sulfate when heated with dilute sulfuric acid. On the basis of the whole of the foregoing data, the formula of taspine may be written out in the following form $C_{26}H_{35}(OCH_3)_2(CH_2O_2)(COO)N(CH_3)_2$.

In approaching the investigation of the structure of the alkaloids isoleontine and leontidine, we decided that we must start by establishing the character of the oxygen-free, saturated heterocyclic substances forming the basis of these alkaloids, and we therefore aimed at securing experimental data that would confirm or disprove the statement [3] that the basis of the alkaloids of lion's tail is the pachycarpine nucleus, and that these alkaloids differ from each other in respect to the arrangement of the carbonyl group, to the presence of double bonds and to the spatial structure. In order to obtain such an oxygen-free saturated compound from leontidine, it was necessary to reduce the carbonyl group and the two double bonds, this was accomplished by catalytic reduction of the alkaloid with platinum catalyst in a hydrochloric acid medium in conditions similar to those for the reduction of the alkaloid thermopsine to α-isosparteine [4].

We worked with leontidine with m.p. 118-119° and $[\alpha]_D$ −192.2°, prepared from the hydrochloride with m.p. 293°. These constants are in accord with those in the literature. Reduction of leontidine was accompanied by absorption of 4.2 moles hydrogen. A liquid, optically active base was obtained which formed well-crystallized salts: monohydroiodide, sulfate, dihydroiodide, perchlorate. The substance does not contain primary or secondary nitrogen atoms and does not change under the action of nitrous acid. Numerous analyses of the base and its salts showed that its composition corresponds to the formula $C_{14}H_{24}N_2$ and not to $C_{15}H_{28}N_2$ as would have been expected on the assumption that the formula of leontidine was $C_{15}H_{28}ON_2$. In spite of the closeness of the analytical values for the possible formulas, the analyses show conclusively that leontidine has a composition corresponding to the formula $C_{14}H_{26}ON_2$. All the analytical data are set forth in Table 2. We see from this table that not one of the results of analysis contradicts the formula $C_{14}H_{26}ON_2$ for leontidine or the formula $C_{14}H_{24}N_2$ for the product of its hydrogenation, apart from which a series of analyses is inconsistent with the formulas $C_{15}H_{28}ON_2$ and $C_{15}H_{26}N_2$.

Consequently leontidine cannot be a member of the sparteine group of alkaloids. The oxygen-free saturated substance on which it is based, for which we propose the name leontidane, is a homolog of sparteine and differs from the latter at the methylene group. It may be suggested that the molecule of leontidane contains 3 six-membered rings and one five-membered ring. We suggest that the establishment of the composition $C_{14}H_{26}ON_2$ for leontidine once more throws doubt on the hypotheses (based only on analogy) of some investigators [2] that leontamine must, in consequence of its occurrence jointly with pachycarpine, possess the composition $C_{15}H_{28}N_2$ and not $C_{14}H_{26}N_2$ as was established by A. P. Orekhov and R. A. Konovalova.

For the purpose of obtaining the oxygen-free saturated skeleton of isoleontine, it was necessary to reduce the carbonyl group to methylene. Our experiments showed that this is easily accomplished by catalytic reduction of isoleontine with platinum catalyst in a hydrochloric acid medium. Apart from the above-mentioned reduction of the carbonyl group of thermopsine, the literature contains other examples of catalytic reduction of carbonyl groups to methylenes [5]. We were unable, however, to find any examples of reduction by this method of carbonyl groups in saturated compounds. Catalytic reduction of isoleontine with platinum catalyst in a hydrochloric acid medium resulted in absorption of 1.9 moles hydrogen. A crystalline, optically active base was obtained which did not contain secondary nitrogen atoms. The substance differs from known compounds of the same composition and we therefore propose for it the name of isoleontane. Isoleontane is an isomer of sparteine. It remains for further research to decide whether the difference between these compounds depends on stereoisomerism or on a more profound structural difference.

EXPERIMENTAL

1.6 kg of dry, pulverized, above-ground parts of the plant were wetted with 10% ammonia solution and exhaustively extracted with dichloroethane. The dichloroethane solution was shaken with 15% sulfuric acid solution. Taspine sulfate came down in the form of a grey precipitate. This was filtered, washed with water and crystallized from 10% aqueous acetic acid (1:150). The first crystallization gave 2.98 g taspine sulfate (0.18% of the weight of the plant) and the second crystallization gave 2.33 g. The filtered acid extract (after separation of the taspine sulfate), with ice cooling, was made alkaline with 25% ammonia solution and exhaustively extracted with chloroform. The chloroform was driven off, leaving a residue of 8.30 g total bases (0.50% of the weight of the plant), in the form of a dark brown oil.

TABLE 2

Leontidine base					Product of hydrogenation of leontidine				
					Base				Hydroiodide
	C	H	N	M		C	H	N	I
$C_{13}H_{19}ON_2$					$C_{13}H_{24}N_2$				
Calculated %	73.71	8.29	11.46	244.4	Calculated %	76.85	11.18	11.95	51.78
$C_{14}H_{18}ON_2$					$C_{14}H_{24}N_2$				
Calculated %	73.04	7.88	12.17	230.02	Calculated %	76.32	10.98	12.72	53.3
Found %	72.73,	7.71,	11.82,	231.4,	Found %	75.91,	11.02,	13.04,	53.84,
	73.12,	7.92,	11.78,	229.8,		75.91,	10.88,	12.96,	53.95
	72.62	8.11				75.67,	10.56,	13.12	
						75.56	10.92		

Isolation of the alkaloids. 830 g total alkaloids was dissolved in 500 ml acetone and acidified with an alcoholic solution of HCl until weakly acid to congo. The crystalline hydrochloride of leontidine (270 g) was thus precipitated. Crystallization from alcohol gave 198 g leontidine hydrochloride with a light-yellow color, m.p. 293°. The organic solvent was distilled off from the hydrochloric acid mother liquors after precipitation and crystallization of leontidine hydrochloride, and then the total bases were separated (500 g). These total alkaloids were subjected to fractional distillation in vacuum at 3 mm; three repetitions of this process gave the following fractions: 1) b.p. 120-150° (35.5g), a light-brown oil; 2) b.p. 171-174° (26 g), a yellow oil, 3) b.p. 175-190° (126 g), a light-yellow oil; 4) b.p. 191-215° (43 g), a viscous, greenish-yellow oil.

The first fraction was once again subjected to vacuum distillation. Two fractions were collected at 8 mm: 3 g with b.p. 126-135° and 28 g with b.p. 136-159°. From the second fraction was obtained a monohydroiodide by dissolving in 5% sulfuric acid solution and adding to the solution (neutral to bromothymol blue) a saturated solution of KI. The precipitated salt, after crystallization from water, melted at 233-234° and did not give a depression with pachycarpine monohydroiodide.

The second fraction was converted into a monohydroiodide by the same procedure as above. Yield 7.9 g salt with m.p. 189-196° (after two crystallizations from water) and $[\alpha]_D$ −44.4°. These constants agree with the constants of L-lupanine monohydroiodide. Further confirmation was obtained by preparing the base and the perchlorate whose constants agreed with those of lupanine base and its perchlorate. Base an optically active crystalline substance, $[\alpha]_D$ −80.70°. The perchlorate has m.p. 212-213° $[\alpha]_D$ −47.8°. Found %: C 51.05, 51.09; H 6.77, 7.10; N 8.26, 8.03. $C_{15}H_{24}ON_2 \cdot HClO_4$. Calculated %: C 51.65; H 7.22; N 8.03. From the mother liquors following separation of L-lupanine hydrochloride no other pure substances could be separated.

The 3rd fraction was dissolved in 200 ml acetone. To the solution was added a saturated alcoholic solution of picric acid until the reaction was acid. Crystalline isoleontine picrate came down and was filtered off and extracted with boiling acetone (twice with 150 ml each time). Yield 75 g finely crystalline powder with m.p. 177-179°. No other pure alkaloids could be isolated from the mother liquors following separation of isoleontine picrate.

The fourth fraction was dissolved in 100 ml acetone. To the solution was gradually added alcoholic HCl until acid to congo. A white crystalline precipitate of a hydrochloride was thus obtained (31.7 g). M.p. (from alcohol) 310-311°. No depression in admixture with leontidine hydrochloride.

Preparation of taspine. After recrystallization from hot water (1:400), taspine sulfate was in the form of thin, white needles which charred at above 360°.

3.110 mg substance: 6.334 mg CO_2, 1.681 mg H_2O. 3.808 mg substance: 7.731 mg CO_2, 1.770 mg H_2O. 8.320 mg substance: 0.241 ml N_2 (24.6° 728 mm). 8.205 mg substance: 0.255 ml N_2 (25.5° 727 mm). 8.275 mg substance: 0.260 ml N_2 (23.5° 727 mm). 5.325 mg substance: 1.620 mg $BaSO_4$ (Carius). 10.560 mg substance: 2.96 ml 0.01 N $Na_2S_2O_3$ (Gelman). Found %: C 55.55, 55.37; H 5.33, 5.20; N 3.18, 3.39, 3.01; S 3.92, 3.99. $C_{13}H_{19}O_2N \cdot 0.5H_2SO_4 \cdot H_2O$. Calculated %: C 55.04; H 5.08; N 3.20; S 3.67.

230 mg taspine sulfate was mixed with 200 ml 10% ammonia solution and the base exhaustively extracted with chloroform. After distilling off the solvent to a small volume, acetone was added to the residue. The base came down in the form of fine white needles which quickly yellowed. Yield 175 g taspine base (0.12% of the weight of the plant). After crystallization from toluene, the base melted at 370°. Taspine is insoluble in water, solutions of caustic alkali and ammonia, alcohol or acetone; it dissolves in chloroform and dichloroethane. The salts with inorganic acids have extraordinarily poor solubility in water. The alkaloid is optically inactive.

3.016 mg substance: 7.171 mg CO_2; 1.346 mg H_2O. 3.809 mg substance: 9.103 mg CO_2; 1.736 mg H_2O. 3.689 mg substance: 8.788 mg CO_2, 1.668 mg H_2O. 6.050 mg substance: 0.213 ml N_2 (24°, 736 mm). 7.385 mg substance: 0.243 ml N_2 (21°, 738 mm). 9.000 mg substance: 0.318 ml N_2 (25.5°, 727 mm). 9.485 mg substance: 15.10 ml 0.02 N $Na_2S_2O_3$. 8.555 mg substance: 13.78 ml 0.02 N $Na_2S_2O_3$. 7.897 mg substance: 12.54 ml 0.02 N $Na_2S_2O_3$. Found %: C 64.85, 65.17, 64.97; H 4.99, 5.10, 5.06; N 3.92, 3.72, 3.86; OCH_3 16.78, 16.66; $N(CH_3)_2$ 11.64. $C_{18}H_{23}O_3N$. Calculated %: C 65.04; H 5.18; N 3.79; $2OCH_3$ 16.80; $N(CH_3)_2$ 11.92.

Taspine methiodide. 0.5 g taspine, 20 ml methanol and 1 ml methyl iodide were boiled on a water bath for 4 hours. During this period the solid changed from light and voluminous to heavy and dense. Crystallization from water (1:750) gave 0.59 g methiodide in the form of colorless, small needles.

3.815 mg substance: 6.696 mg CO_2; 1.715 mg H_2O. 3.481 mg substance: 6.105 mg CO_2; 1.500 mg H_2O. 7.000 mg substance: 0.163 ml N_2 (24°, 728.5 mm). 5.202 mg substance: 6.0 ml 0.02 N $Na_2S_2O_3$. 5.202 mg substance: 7.98 ml 0.02 N $Na_2S_2O_3$. Found %: C 47.87, 47.83; H 5.03, 4.82; N 2.57; OCH_3 11.92; $N(CH_3)_2$ 11.4. $C_{18}H_{23}O_3N \cdot CH_3I \cdot H_2O$. Calculated %: C 47.65; H 4.57; N 2.64; $2OCH_3$ 11.82; $N(CH_3)_2$ 11.15.

Alkaline hydrolysis of taspine. 0.4 g taspine base was boiled for 15 minutes with 70 ml 0.1 N NaOH solution; the base gradually went into solution. Acidification of the cooled solution with sulfuric acid until the reaction was acid to congo resulted in precipitation of fine white crystals of amino acid. The precipitate was filtered off, crystallized from 5% acetic acid solution and dried in vacuum (8 mm) at 83°. The substance was soluble in solutions of caustic alkali and ammonia and was not extracted from these solutions by organic solvents and was not brought down by saturated carbon dioxide solution.

3.159 mg substance: 6.862 mg CO_2, 1.614 mg H_2O. 4.122 mg substance: 8.900 mg CO_2, 2.247 mg H_2O. 6.340 mg substance: 0.196 ml N_2 (22°, 736 mm). Found %: C 59.24, 58.89; H 5.72, 6.10; N 3.46. $C_{18}H_{21}O_5N \cdot H_2O$. Calculated %: C 59.20; H 5.71; N 3.45.

The substance went into solution when heated with 10% sulfuric acid solution; on further heating and boiling taspine sulfate was precipitated, insoluble in solutions of caustic alkalies and ammonia. The taspine sulfate was mixed with 10% ammonia solution and the base was extracted with chloroform. The chloroform was driven off and the base recrystallized from toluene.

Found %: C 65.22, 65.03; H 5.41, 5.36; N 4.02, 3.87. $C_{18}H_{19}O_4N$. Calculated %: C 65.04; H 5.18; N 3.79.

Preparation of leontidine. 1.8 g leontidine hydrochloride was dissolved in a small quantity of water. The solution was made alkaline with 4.0% NaOH solution and the base repeatedly extracted with ether. The ethereal extract was dried with anhydrous sodium sulfate and the solvent completely removed. The residue was 1.32 g viscous, light-yellow oil which crystallized on standing. After two recrystallizations from a mixture of benzene and ether (1:4), colorless base melted at 118-119°.

0.1737 g substance: 10 ml methyl alcohol, l 1 dm, α_D −3.34°; $[\alpha]_D$ −192.2°. 3.107 mg substance: 8.281 mg CO_2, 2.142 mg H_2O. 3.988 mg substance: 10.639 mg CO_2; 2.900 mg H_2O. 4.745 mg substance: 0.490 ml N_2 (21°, 749 mm). 4.728 mg substance: 0.498 ml N_2 (23°, 734 mm). 0.4234 mg substance: 18.20 ml 0.1 N HCl (methyl red). 0.4299 mg substance: 18.70 ml 0.1 N HCl (methyl red). Found %: C 72.73, 72.62; H 7.71, 8.11; N 11.82, 11.73; equiv. 231.4, 229.8. $C_{18}H_{21}O_4N$. Calculated %: C 73.01; H 7.88; N 12.17; equiv. 230.2.

Leontidine hydrochloride. A crystalline precipitate was formed on mixing alcoholic solutions of leontidine and hydrochloric acid. M.p. of hydrochloride 310-311° (after recrystallization from alcohol).

3.743 mg substance: 8.163 mg CO_2; 2.541 mg H_2O. 3.923 mg substance: 8.557 mg CO_2; 2.669 mg H_2O. 5.146 mg substance: 0.450 ml N_2 (23°, 734 mm). 8.169 mg substance: 5.85 ml 0.01 N H_2SO_4 (Kjeldahl). 7.854 mg substance: 3.966 ml 0.1 N $AgNO_3$. 7.460 mg substance: 3.847 ml 0.1 N $AgNO_3$. Found %: C 59.51, 59.52; H 7.60, 7.61; N 9.74; 10.02; Cl 12.48, 12.75. $C_{18}H_{20}ON_2 \cdot HCl \cdot H_2O$. Calculated %: C 59.04; H 7.43; N 9.84; Cl 12.45.

Preparation of isoleontine. 62 g isoleontine picrate was treated with an 18% solution of HCl. The separated picric acid was filtered off and washed with dilute hydrochloric acid. The filtrate and the wash liquor were extracted with ether until the whole of the picric acid was removed. The acid solution was cooled with ice, made alkaline with 40% NaOH solution and exhaustively extracted with ether. The ethereal extract was dried with anhydrous sodium sulfate and evaporated down to a small volume. Crystalline isoleontine came down (24.3 g). Two crystallizations from ether gave 20 g isoleontine in the form of small, colorless crystalline needles with m.p. 107-108°.

0.4318 g subs.: 3.1 ml abs. alcohol, $\underline{l}$ 0.5 dm; α_D −5.45°; $[\alpha]_D$ − 78.2°.

3.940 mg substance: 10.458 mg CO_2; 3.350 mg H_2O. 4.062 mg substance: 10.810 mg CO_2; 3.422 mg H_2O. 5.338 mg substance: 0.517 ml N_2 (21.5°, 734 mm). 5.327 mg substance: 0.517 ml N_2 (21.5°, 734 mm). Found %: C 72.44, 72.62; H 9.51, 9.43; N 10.83, 10.85. $C_{18}H_{24}ON_2$. Calculated %: C 72.55; H 9.74; N 11.28.

Isoleontine base is easily soluble in water and in all common organic solvents except hexane and ligroine.

Isoleontine perchlorate was prepared by adding a saturated aqueous solution of magnesium perchlorate to a solution of isoleontine in 5% HCl. After recrystallization from water it melted at 252° (with decomposition).

3.405 mg substance: 0.249 ml N_2 (20°, 742 mm). 6.023 mg substance: 0.422 mg N_2 (18°, 742 mm). Found %: N 8.32, 8.02. $C_{18}H_{24}ON_2 \cdot HClO_4$. Calculated %: N 8.03.

Isoleontine methiodide. To a solution of isoleontine in acetone was added methyl iodide. Crystalline isoleontine methiodide came down on standing. After crystallization from alcohol (1:3) it melted at 297° (with decomposition).

4.035 mg substance: 6.33 ml 0.01 N $Na_2S_2O_3$. 3.944 mg substance: 6.06 ml 0.01 N $Na_2S_2O_3$. Found %: I 33.20, 32.51. $C_{18}H_{24}ON_2 \cdot CH_3I$. Calculated %: I 32.51.

Hydrogenation of leontidine. 6 g leontidine with m.p. 118-119° was dissolved in 360 ml 1 N HCl; to the solution was added 2.27 g platinum oxide and the whole shaken in a hydrogen atmosphere under a small pressure. After 2 $\frac{1}{2}$ hours 2.5 liters hydrogen had been absorbed (4.2 moles), and the absorption was concluded. The catalyst was thereupon filtered off and the solution made alkaline with 40% NaOH solution and exhaustively extracted with ether. The ethereal extract was dried with anhydrous sodium sulfate and the solvent completely driven off. The residue of 5.6 g light yellow oil was neutralized with 5% sulfuric acid solution (bromothymol blue indicator), the solution was filtered and to the filtrate was added a saturated solution of KI. The crystalline monohydroiodide immediately came down (4.6 g). Recrystallization from water gave 4.1 g of a white, lustrous crystalline powder which melted at 219-220°.

0.1858 g substance: 3 ml alcohol $\underline{l}$ 0.5 dm; α_D + 0.32°; $[\alpha]_D$ + 10.33°.

Leontidane base. 4.8 g of the monohydroiodide was dissolved in water and excess of 40% NaOH was added. The alkaline solution was exhaustively extracted with ether, the ethereal extract was dried with anhydrous sodium sulfate, and the ether completely driven off to leave 2.5 g of liquid leontidane base. This distils in vacuum at 141-144° (5 mm). The base dissolves readily in all the common organic solvents.

$\underline{l}$ 0.5 dm; α_D −3.88°; $[\alpha]_D$ −7.7° (without solvent). 0.3028 g subs.: 5 ml alcohol, $\underline{l}$ 0.5 dm; α_D + 0.5°; $[\alpha]_D$ + 16.5°.

3.596 mg subs.: 10.002 mg CO_2; 3.543 mg H_2O. 4.332 mg subs.: 12.051 mg CO_2; 4.212 mg H_2O. 6.308 mg subs.: 0.729 ml N_2 (21°, 734 mm). 6.537 mg subs.: 0.735 ml N_2 (21°, 734 mm). Found %: C 75.91, 75.91; H 11.02, 10.88; N 12.96, 13.12. $C_{18}H_{26}N_2$. Calculated %: C 76.32; H 10.98; N 12.72.

Leontidane sulfate. 0.5 g base was dissolved in 1 ml absolute alcohol and 10% sulfuric acid solution in absolute alcohol was added until the reaction was acid to congo. Addition of a small amount of acetone brought down white crystals which deliquesced in the air. M.p. 229-230°.

0.1538 g subs.: 3 ml alcohol, $\underline{l}$ 0.5 dm; α_D + 0.5°; $[\alpha]_D$ + 19.5°.

Leontidane dihydroiodide. Mixing of alcoholic solutions of the base and hydriodic acid (acid reaction to congo) caused a crystalline precipitate to appear. After crystallization from alcohol the salt melted at 268° (with decomposition).

4.802 mg substance: 12.22 ml 0.02 N $Na_2S_2O_3$. 3.200 mg substance: 8.16 ml 0.02 N $Na_2S_2O_3$. Found %: I 53.84, 53.95. $C_{18}H_{26}N_2 \cdot 2HI$. Calculated %: I 54.0

Leontidane perchlorate was prepared by adding magnesium perchlorate to a solution of the base in 5% sulfuric acid. M.p. (from 90% alcohol) 234°.

0.1547 g subs.: 3 ml water, l 0.5 dm; α_D + 0.53°; $[\alpha]_D$ + 20.55°.

5.201 mg subs.: 0.283 ml N_2 (17.5°, 734 mm). 5.139 mg subs.: 0.295 ml N_2 (18°, 733 mm). Found %: N 6.18, 6.49; $C_{15}H_{24}N_2 \cdot 2HClO_4$. Calculated %: N 6.67.

Hydrogenation of isoleontine. 1.8 g isoleontine (m.p. 107-108°) was dissolved in 100 ml 1 N HCl solution and 0.86 g platinum oxide was added. On shaking in a hydrogen atmosphere for 14 hours, 310 ml (1.9 moles) hydrogen was taken up. At the termination of hydrogenation the catalyst was filtered off and the solution made alkaline with 40% NaOH solution and exhaustively extracted with ether. The extract was dried with solid KOH and the solvent driven off to leave 1.65 g yellowish crystals with m.p. 68-72°. After two crystallizations from ether (1:3) the base melted at 77-78.5°. Readily soluble in water and alcohol, less soluble in ether and acetone. 0.1634 g subs.: 3.05 ml abs. alcohol: l 0.5 dm; α_D −0.81°; $[\alpha]_D$ −30.1°.

4.091 mg subs.: 11.559 mg CO_2; 4.001 mg H_2O. 3.709 mg subs.: 10.453 mg CO_2 3.699 mg H_2O. 4.830 mg subs.: 0.487 ml N_2 (23°, 748 mm). 4.865 mg subs.: 0.500 ml N_2 (23.5°, 732 mm). Found %: C 77.11, 76.91; H 10.94, 11.15; N 11.44, 11.40. $C_{15}H_{26}N_2$. Calculated %: C 76.85; H 11.19; N 11.95.

Isoleontane picrate was prepared by mixing alcoholic solutions of the base and picric acid. M.p. 256° (with decomp.) after crystallization from 1:1 alcohol-acetone.

Isoleontane hydrochloride. Prepared in the form of slender needles by adding alcoholic HCl to an alcoholic solution of the base until the reaction was acid to congo. After crystallization from acetone-alcohol (1:1 mixture) and drying at 105° the hydrochloride melted at 368° with considerable sublimation.

0.1709 mg subs.: 3 ml alcohol; l 0.5 dm; α_D −0.42°; $[\alpha]_D$ −14.7°; 3.860 mg subs.: 7.959 mg CO_2; 3.291 mg H_2O; 4.358 mg subs.: 8.943 mg CO_2; 3.619 mg H_2O. 4.389 mg subs.: 0.342 ml N_2 (22°, 733 mm). 6.351 mg subs.: 0.488 ml N_2 (22°, 733 mm). 7.630 mg subs.: 6.817 ml 0.1 N $AgNO_3$. 7.945 mg subs.: 6.955 ml 0.1 N $AgNO_3$. Found %: C 56.27, 56.00; H 9.54, 9.29; N 8.70, 8.58; Cl 22.10, 21.66. $C_{15}H_{28}N_2 \cdot 2HCl \cdot H_2O$. Calculated %: C 55.38; H 9.29; N 8.61; Cl 21.80.

Isoleontane methiodide. To a solution of the base in acetone was added MeI. On standing, a crystalline precipitate appeared which melted (from 75% alcohol) at 292° (with decomp.)

0.1093 g subs: 2.9 ml water, l 0.5 dm; α_D −0.1°; $[\alpha]_D$ −5.3°.

SUMMARY

1. A new alkaloid with the composition $C_{28}H_{48}O_6N$, named taspine, was isolated from Leontice Ewersmannii Bge.

2. An alkaloid $C_{15}H_{26}ON_2$ was isolated which differs from leontine in optical activity and was named isoleontine.

3. The alkaloid leontidine was found to have the composition $C_{14}H_{24}ON_2$ and not $C_{15}H_{26}ON_2$.

4. From leontidine $C_{14}H_{24}ON_2$ and isoleontine $C_{15}H_{26}ON_2$ were prepared the hydrogen free saturated compounds leontidane $C_{14}H_{26}N_2$ and isoleontane $C_{15}H_{28}N_2$.

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* See Consultants Bureau, English Translation, p. 1425 ff.